Driving genetic research forward

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A light at the end of the tunnel

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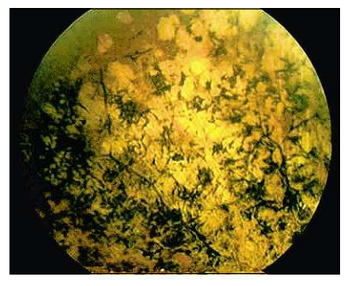

TCD Geneticsat50

A SPECIAL REPORT

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Solving the secrets of life through genetic research

JAMES WATSON

Trinity College has played a critical role in unravelling the mysteries of DNA since its Department of Genetics was established in 1958

THE ESTABLISHMENT of the Department of Genetics in 1958 at Trinity College was a key step in helping Ireland emerge as a knowledge-based economy, as opposed to an agriculture-based economy. With DNA-based thinking becoming an ever-increasing prerequisite for modern life, Trinity can take great comfort that it saw the future early and ran with it.

Ireland had a major role in modern biology that long predated the 1953 discovery by Francis Crick and me of the double helical structure of DNA, the chemical that carries the genetic information of chromosomes.

Key to tackling the essence of biological macromolecules like proteins and the nucleic acids, DNA and RNA, was the development of X-ray crystallographic methodologies for determining the 3-D arrangement of their atoms.

The extraordinary, Tipperary-born John Desmond Bernal was the first to jump in. In the late 1920s, as an undergraduate at Cambridge, he established the multiple symmetries through which molecules came together in crystals.

Then, as a member of the staff of its already famed Cavendish Laboratory, he and his student Dorothy Crowfoot Hodgkin obtained, in 1933, the first X-ray photos of crystalline proteins. Under his supervision soon after was the Austrian-born, young chemist Max Perutz, whose lifelong objective became the study of the oxygen-carrying protein hemoglobin. After the war, Perutz shrewdly headed the Cavendish's MRC Unit for the study of Biological Structures.

It leads the world in the number of Nobel Prizes awarded to members of its staff, including ones for Perutz and his close colleague John Kendrew, whose research focused on the much smaller oxygen-carrying protein, myoglobin. Equally important, neither Crick, nor I, nor the New Zealand-born Maurice Wilkins, whose parents came from Ireland, and whose father was a Trinity doctor, would have shared the 1962 Nobel Prize in physiology or medicine had we all not changed our intellectual goals after our 1946 readings of *What is Life?* by the 1933 Nobelist Erwin Schrödinger, the inventor of wave mechanics. Before a Trinity College audience in 1943, he gave three lectures that soon formed the heart of a highly influential little book. Then a refugee from Hitler's Austria at Dublin's Institute of Advanced Studies, he looked at life from the viewpoint of a physicist – concluding that its essence must be an information-bearing molecule residing in chromosomes that had the form of an aperiodic crystal.

After their independent readings of *What is Life?*, Crick gave up physics to study cells in culture at Cambridge, while Wilkins moved from physics to DNA research at King's College London. There, in its new biophysics lab, he used X-ray methodologies to show that DNA did indeed have a quasi crystalline-like structure.

Hearing of this bombshell at a small May 1951 meeting in Naples, I, until that moment a pure biologist, saw the need to quickly reeducate myself as a crystallographer through going to the Perutz-led MRC Unit at Cambridge. There, Crick had come two years before in search of life's crystallographic mysteries.

Then a key player in the newly emerging discipline of bacterial genetics was the recently London-based, Trinity-educated, medical microbiologist William (Bill) Hayes. I first encountered his keen intelligence and drive at a September 1952 microbial genetics gathering at Pallanza on Lake Maggiore in Italy. That fall, at Hammersmith Hospital, we began writing a research paper explaining unexpected patterns of genetic recombination in the bacteria E.coli. My thoughts, however, quickly turned back to DNA through learning that the great American chemist Linus Pauling's focus had turned from proteins to DNA.

Realising that Pauling's new triple helix for DNA was wrong, I went to London to tell Wilkins that DNA was yet to be won. From him I learned that his colleague, Rosalind Franklin, had passed on to him a hitherto undisclosed X-ray photo that unambiguously revealed an underlying helical conformation for DNA. Only a month then passed before Crick and I found the Double Helix with its two chains bearing complementary sequence information in its base pairs (A=T and G=C).

The finding of the Double Helix soon made bacterial genetics much easier to interpret, helping Hayes write his magisterial *The Genetics of Bacteria and their Viruses* by 1964. Bacterial genetics first came to Trinity College through the arrival in 1950 of George Dawson, fresh from Cambridge University, where he learned how to do microbial genetics from the Caltech – and Stanford-trained David Catcheside, and was influenced by Ronald Fisher, the very great quantitative geneticist and statistician.

In Dublin, his first student, Stewart Glover, after further training in the US, moved to London with Hayes and from there to Newcastle where he became its first professor of genetics.

Dawson's focused infectious enthusiasm for genetics led to his heading, in 1958, of Trinity's Department of Genetics. From the start, Dawson saw his department pursuing both pure and applied genetics. In 1962, he appointed Patrick Cunningham of the Agricultural Institute to teach quantitative genetics, the underpinning of scientific plant and animal breeding programs. Later, Vincent Connolly of the Agricultural Institute came on board to teach plant genetics.

Equally far-reaching was his appointment to the staff of Peter Smith Keary, who taught with Dawson a challenging undergraduate degree program in genetics.

Together they led a tiny group of students in research on mutations in bacteria. Under them, John Atkins and Shahla Thompson began their extraordinary work on frameshift mutations that alter the reading of the Genetic Code.

From Trinity, Atkins went to study protein synthesis in Cold Spring Harbor before returning to his lifelong obsession with the Genetic Code at Salt Lake City and now at Cork.

When the recombinant DNA methods for isolating genes became available in the 1970s, Trinity was already positioned for its biotechnology application through the presence of its graduate, David McConnell, whose years abroad at the California Institute of Technology and Harvard let him be among the first to make restriction enzymes and sequence long stretches of DNA.

Soon, worldwide cries for moving DNA sequencing from genes to genomes (all the DNA of an organism) led to the initiation of the internationally organised Human Genome Project in 1988.

It aimed to complete the human DNA sequence by 2003, at a cost of $3 billion (around €2.1 billion). Playing a key role in its ultimate success was the Trinity graduate in biochemistry, Michael Morgan.

After joining the Wellcome Trust in London as a research administrator, he oversaw the speedy construction of its massive Sanger Center outside Cambridge.

Over 30 per cent of the human genome was assembled there. Later, Morgan organised the key 1996 gathering of genome scientists in Bermuda that made the far-sighted decision to make all DNA sequence data available on the web as soon as it was obtained. Through this meeting, public ownership of human DNA sequences was assured.

Trinity scientists have played key roles in sequencing and analysing genomes of bacteria, yeasts and plants, as well as the genome of humans. The vast amount of sequence data generated by genome-level DNA sequencing projects has lead to the emergence of the fast-moving discipline of Bioinformatics. At Trinity, Paul Sharp took on this challenge working with McConnell on one of the first known genomes, that of the bacterial virus T7.

Later, Sharp moved on to the evolution of the HIV virus. Now in Edinburgh, his legacy is a team of outstanding Trinity graduates, who focus on how DNA has evolved since it first emerged as the primary genetic molecule several billion years ago.

At Trinity, Peter Humphries and Jane Farrer used some of the first human genetic markers to locate a gene behind retinitis pigmentosa, soon following up their breakthrough to find several more mutant genes that lead to human blindness.

Trinity much enhanced its future in genetics when Sir Michael Smurfit provided funds to endow a chair in Medical Genetics, currently held by Seamus Martin.

Now radically changing the way genetics will be done over the future are the rapidly diminished costs of DNA sequencing. Previously inherently intractable problems, like the gene changes behind schizophrenia, can soon be solved. Leading this challenge at St James's Hospital in Dublin is Michael Gill, whose genetics career focuses on psychiatric disorders.

Genetics at Trinity, perhaps through its new focus on neurogenetics, will continue to move fast and be far-reaching to the great benefit not only of the people of Ireland, but of the whole world.

■ James Watson is one of the co-discoverers of the double helix structure of DNA.

A sculpture of the double helix by Brian King that stands outside the Smurfit Institute of Genetics at TCD

> With DNA-based thinking becoming an ever-increasing prerequisite for modern life, Trinity can take great comfort that it saw the future early

Winning discoveries: Genetics and the Nobel prize

NOBEL PRIZES show how sciences emerge. Genetics developed slowly at first but has expanded rapidly since the momentous discovery of the structure of DNA in 1953. That opened up a new phase of genetics, often called "molecular biology" or "molecular genetics", in which scientists study the behaviour of genes at the molecular level.

Molecular genetics led to "genetic engineering", a set of tools that are used in every branch of biological research today. These tools were the key to modern biotechnology, which in turn is revolutionising society through its impact on medicine, agriculture and forensics.

Until 1953 only five Nobel prizes were awarded which related to genetics.

We can count about 10 major discoveries in that early period. Mendel identified genes in 1866, but we had to wait till 1901 for the discovery that genes are located on chromosomes. Then it was discovered, in 1911, that maps can be made of genes on chromosomes, that specific genes code for specific proteins in 1941 and, in 1944, that genes are made of DNA.

In 1953 Watson and Crick discovered that the DNA molecule was a double helix, capable of carrying a huge amount of code, capable of dictating its own replication and capable of evolving by mutation.

After 1953 there were about 30 momentous discoveries that

affected the understanding of genes, how they work, how they are transmitted, how they have evolved and how and why they cause illness.

Many of these discoveries were not at all predictable in 1953. Few foresaw the evidence that some genes are repeated many times side by side, that genes may be split by non-coding sequences, that genes can jump from one place to another on chromosomes, that genes jump between species, that genes can be programmed to mutate during development (in the immune system), that the rate at which genes evolve is driven by mutation and drift, that DNA sequences could be used to date the origin of man, or that infectious particles called prions have no DNA or RNA.

Furthermore, none expected that the basic human genetic code would be known by 2003, and that it only contains about 20,000 standard genes.

This flood of discoveries is reflected in the awarding of the Nobel prize in medicine on more than 30 occasions for work that was important in genetics.

In the same period the Nobel prize in chemistry has been awarded on 10 occasions for work related closely to genetics.

One prize in peace was awarded in 1970 to the geneticist Norman Borlaug, who masterminded the Green Revolution. More Nobel prizes are keenly awaited – perhaps in human genetics or even in neurogenetics.

Academic excellence attracts innovation

KARLIN LILLINGTON

IRELAND MAY be small, but it is increasingly attracting an international spotlight when it comes to research and commercial activity in the life sciences. Consider the evidence: among European nations, the state attracted one-quarter of all foreign direct investment in the life sciences last year. It has over 170 companies in the sector, employing over 35,000 people. Its life sciences exports totalled close to €40 billion last year.

Ireland has leading researchers and research groups on the international stage. Trinity College's genetics and molecular biology researchers, for example, have been ranked seventh worldwide in terms of citations in other publications.

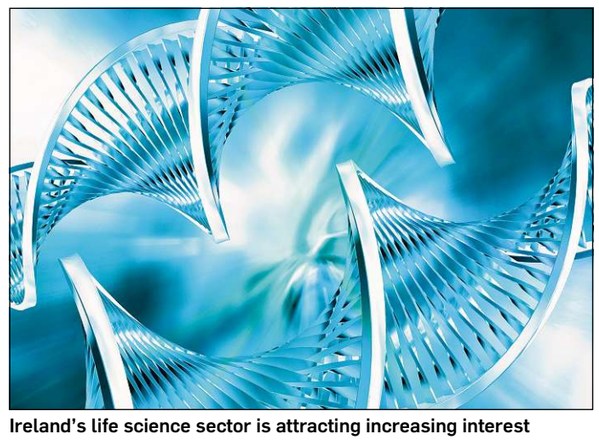
Not that this success has come easy – until 1998, when the then government published its *Foresight* report that changed the landscape of investment, promotion and funding of scientific research in Ireland, only tiny amounts of support were available to the life sciences sector, says Paul Roben, Enterprise Ireland's director for Bio in Life Sciences.

After the publication of *Foresight*, the establishment of Science Foundation Ireland (SFI) and growth in other research supports, life sciences were given an enormous boost. Life sciences and genetics research in particular have become a "significant" niche sector for Ireland Inc, says Roben.

For the Government, and agencies like Enterprise Ireland, a key concern has been to convert research into commercial applications. "This is what it is all about – creating high-value jobs," says Roben.

Hence the increased focus within third level on supporting researchers and helping them spin out companies that drive job growth and further investment. TCD's genetics department has already seen two high-profile companies move from its halls to the global life sciences scene, Genable and IdentiGEN.

Having a base of well-regarded, science-focused companies also helps raise Ireland's overall international profile, adds Roben. And that, in turn, makes the Irish Development Agency's (IDA's) job easier – a solid research and business profile helps attract foreign inward investment.



Ireland's life science sector is attracting increasing interest

At home, great researchers, strong publications and a steady stream of new companies helps the university attract funding.

"Strong researchers help a lot," says Zhanna O'Clery, associate director of the Trinity Foundation, which fundraises for the university. "They are visionaries and you can leverage funding on to the grants they get.Having top researchers gives us the advantage of showing great potential for achievement – excellence attracts funding," she says.

"That's why it's important for us to have top scientists to demonstrate vision, that have the ability to communicate their ideas."

Funding from multinational corporations is relatively small, she says. TCD receives major grants and donations from research trusts such as the Wellcome Trust, from bodies such as SFI and from Europe.

In addition, individual philanthropists donate varying amounts. "You try to match their interests and engage with the donor."

Within a department, excellence also attracts excellence, says David McConnell, professor of genetics at TCD and chairman of The Irish Times Trust.

"You start with the international reputation of a person on the faculty who might have published something that comes to public attention," he says. Those achievements help draw top students, postgraduates, researchers, and grants to the institution.

And in the case of a young company, a high-profile individual helps secure interest from investors and other supports.

Every year TCD loses some of its bright sparks as they head into the world of business with their young companies, he says. "But what matters is how many brilliant people are coming in."In other words, it is today's students, postgraduates and researchers who will be building tomorrow's TCD – and tomorrow's Ireland Inc.

TCDGeneticsat50 A SPECIAL REPORT

Support for genetics guarantees a lasting legacy

Over the past 50 years, Trinity's Department of Genetics has benefited from the gifts of a distinguished and imaginative group of research supporters. **Louise Holden** reports on their significant contributions

The generosity of Trinity's benefactors in genetics allows this work to continue to the present day. Photograph: Getty Images

THE DEPARTMENT of Genetics at Trinity College Dublin has a distinguished lineage of benefactors that can be traced back to a £15,000 donation by the Irish Sugar Company in 1957. On the initiative of Lt Gen Michael Joseph Costello, this funding allowed for the establishment of the 50-year-old faculty in the former home of St Mark's Hospital, Sir William Wilde's Ophthalmic Hospital for Diseases of the Eye and Ear.

So it was remarkable that a small group of blind and vision-impaired people, RP-Ireland Fighting Blindness, led by Michael Griffith, started to fund research in Trinity in 1985 on the genetics of retinitis pigmentosa.

Prof David McConnell of the Institute of Genetics says that their support was critical in the development of genetics research at Trinity.

In 1987, they raised the then colossal sum of £100,000 to promote the research by Peter Humphries and Jane Farrar.

In 1989, Dr Michael Smurfit, perhaps influenced by the success

> The unselfish support of scientists and philanthropists continues to bolster the work of the institute to this day

of the research on blindness, enhanced the standing of the department further when he endowed Trinity with the Smurfit Chair of Medical Genetics, a gift to commemorate the 400th anniversary of the university (1992).

Ten years later, four major benefactors made contributions which matched money from the EC, and enabled the creation of the new Institute of Genetics, to be housed in a custom-designed facility on the old St Mark's Hospital site.

Chuck Feeney, founder of Atlantic Philanthropies, made the first gift. He later revolutionised research in Ireland when he decided, a decade ago, to recruit the Government as a partner in launching the Programme for Research in Third-Level Institutions (PRTLI).

Dr Martin Naughton is executive chairman of Glen Dimplex, one of the world's largest manufacturers of small electrical appliances.

Naughton is an imaginative supporter of research in Ireland, and has supported the Naughton Institute for Nanotechnology at TCD, as well as the Naughton Chair in Business Strategy at Queen's University Belfast, and the National Gallery of Ireland.

His contribution to the establishment of the Institute of Genetics in 1996 was one of the earliest examples of his commitment to developing world-class research in the arts, sciences and social sciences in this country.

Dr Smurfit is well-known for his philanthropic commitments to Irish academia – the UCD School of Business is named for him, and he has been involved in supporting the development of genetics research in Trinity for almost 20 years.

The Wellcome Trust established a competitive fund for capital development in biomedical science in Ireland; Trinity's proposal for the Institute of Genetics was generously supported.

Thanks to the generosity of these four patrons, the new Smurfit Institute of Genetics came to be. Designed by Scott, Tallon and Walker, and built by Bernard MacNamara, the 5,000-square metre bespoke facility was opened by the then taoiseach Bertie Ahern in 1998.

The unselfish support of scientists and philanthropists continues to bolster the work of the institute to this day.

Prof George Dawson, one of the founders of the faculty, established the TCD Dawson Prize in Genetics, awarded for the first time in 2006 to Nobel Prize winner Dr John Sulston.

The department flourished. In 1975 it received a boost when Dr AWB Vincent instituted the Vincent Scholarships to support third-year genetics students in summer studies in American laboratories.

Vincent's scholarships continue to benefit students today, with six undergraduates travelling to the US every year.

The experience is valuable insofar as it exposes students to new ideas and avenues of enquiry. According to McConnell, it has an equally profound effect on their confidence in what they already know.

"By travelling in the US, our students tend to discover that their level of knowledge is as high if not higher than their contemporaries in the US. This is very encouraging for them as they return to their studies for their final year at Trinity. Many decide to become researchers as a result of their US experiences," says McConnell.

Over the past four years, individual research projects at the Institute of Genetics have attracted considerable support from Science Foundation Ireland (SFI). Each project is considered by SFI on merit, but, given the global status of the institute and the calibre of work there, TCD's genetics faculty submit strong applications to the Government's main science research investment body.

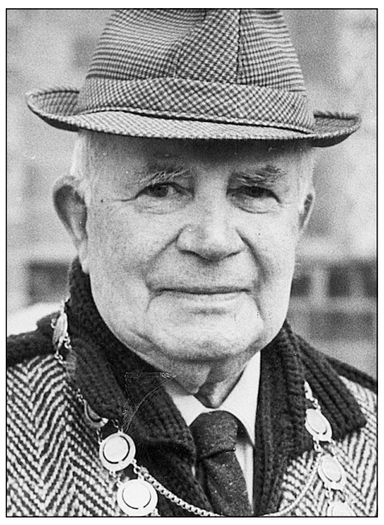
The institute has also received donations towards the development of clinical genetics from the Adelaide Hospital Society and the National Children's Hospital. The building itself is ageing gracefully, thanks in part to the aesthetic sensibility of key donors.

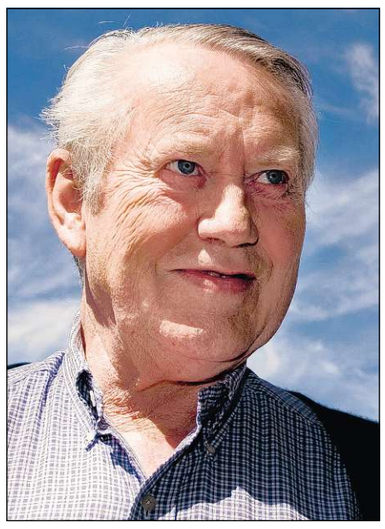
Dr Beate Schuler donated a sculpture of the double helix, by Brian King, to commemorate (in 2003) the 50th anniversary of Watson's and Crick's discovery.

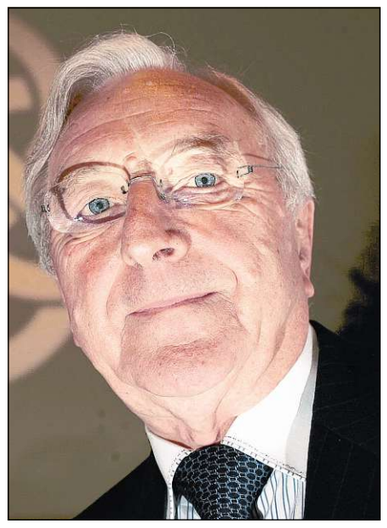
Prof Laurence Roche gave a painting by Dr Arnaldo Pomodoro, and the artist himself presented a set of graphic works to display in the new foyer.

Dr Ronnie Tallon, the building's architect, and George Dawson, gave a most apposite gift – a bust by Melanie le Brocquy of Oscar Wilde, son of Sir William Wilde.

TRINITYBENEFACTORS VISIONARIES





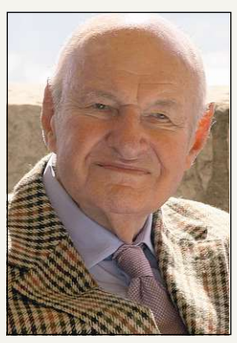


LT GEN MICHAEL JOSEPH COSTELLO (far left) Costello was instrumental in the donation of £15,000 by the Irish Sugar Company in 1957, allowing for the establishment of the now 50-year-old genetics faculty

CHUCK FEENEY (centre) Feeney, founder of Atlantic Philanthropies, was one of four benefactors who matched money from the EC enabling the creation of the Institute of Genetics at TCD

DR MARTIN NAUGHTON (left) Naughton's contribution to the establishment of the Institute of Genetics in 1996 was one of the earliest examples of his commitment to developing world-class research in this country

Benefactor profile AWB Vincent



IN 1975, AWB Vincent (born at Muckross House, Killarney) established the Vincent Scholarships, designed to support third-year genetics undergraduates at Trinity College Dublin to travel to US laboratories to study in the summer months.

This legacy continues to enhance the academic development of students. Every year, six undergraduate students spend three months studying new methods and sharing expertise in leading genetics laboratories across the Atlantic.

Nowadays, these undergraduates have plenty to offer, because the TCD Institute of Genetics ranks among the leading genetics research centres in the world. Vincent was a founding member of the American Irish Foundation. The foundation partnered with Ireland Funds in 1983, forming the American Ireland Fund. In the meantime, Vincent extended his philanthropic work into Germany, France and the UK.

– Louise Holden

Benefactor profile Wellcome Trust

THE WELLCOME Trust supports the work of researchers all over the world who work to improve human and animal health. The Trust awards £600 million (€753 million) every year to a range of projects covering biomedical research, technology transfer, medical humanities and activities that promote a better public understanding of science.

The trust was instrumental in the establishment of TCD's Institute of Genetics, opened in 1998. The Wellcome Trust saw fit to support the establishment of the new institute, but already had a well-established funding relationship with TCD, according to Michael Morgan **(pictured right)**.

"Irish researchers can apply to the Wellcome Trust for funding in the same way as their UK counterparts," says Morgan, formerly of Wellcome Trust. "Trinity has done well in terms of competitive grants, because the standard of the research is outstanding. In addition to awarding the grant for the new institute, we have a long history of awarding grants to TCD to support the work of researchers such as Peter Humphries."

Morgan is a former student of Trinity College Dublin, who graduated in 1965 with a degree in biochemistry. He went on to a PhD programme at the University of Leicester and carried out his post-doctoral research in the US. Upon his return to the UK, he helped to set up the New Blood scheme with the Irish Government, to support the work of young researchers here.

In the early 1990s, Morgan got involved in the Human Genome Project, through his involvement with the Wellcome Trust.

"The Wellcome Trust linked with the Human Genome Project through the work of John Solstun," Morgan explains. "Sir John Sulston, founder and director of the Sanger Institute in Cambridge University, argued that sequence data from the human genome should be freely available to international researchers, and should be released as quickly as possible."

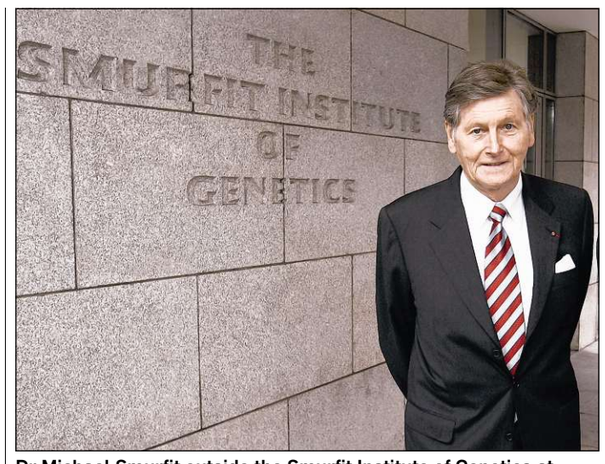
Funding from the Wellcome Trust for the Human Genome Campus in the Sanger Institute in Cambridge has ensured genome sequence information generated by Sulston and others can be accessed by researchers all over the world.

One-third of the human genome has been sequenced at the Sanger Institute as part of the Human Genome Project.

"When the human genome was first sequenced it cost about $400 million [about €283 million]," says Morgan. "Now we can do a sequence for less than $1 million [€700,000]. Eventually, we think it should cost around $1,000 [€707].

"As more individual genomes are being sequenced, human genome variation can be studied and linked to all sorts of potential health outcomes such as heart disease and obesity. It has to be an international process – not even the US has a large enough sample to allow for comparison. We need to share 'biobanks' all over the world. An Irish biobank is at the planning stage, I hear."

– Louise Holden



Dr Michael Smurfit outside the Smurfit Institute of Genetics at Trinity College Dublin. Photograph: Mac Innes

Matching evolution with adaptation

TCD benefactor Michael Smurfit talks proudly of the developments in genetics research via the Smurfit Institute and his belief that Ireland can continue to lead the field in this area

'IT HAS been through the efforts and ingenuity of the staff and students at TCD that genetics has become the resounding success it is today. The Chair of Medical Genetics I endowed in 1989 in preparation for the quatercentenary of the college, on the suggestion of Provost Watts, had been a great success and so it was natural that I should respond when Provost Mitchell asked me to help to fund the new institute in 1997.

"Ten years on, I feel very much the distinct honour of having this institute and the chair carry the Smurfit name.

"I first became interested in supporting genetics after speaking to Provost Watts and other people about the area. I soon realised that whether it is cardboard boxes or indeed biotechnology, many of the basic principles of strategy, individual thinking and entrepreneurship have the same relevance and role.

"While the institute's role in research and teaching has given it recognition as one of the top science research institutes in the country and it ranks amongst the world leaders in genetics, what is equally pleasing is how some of the practical applications of that crucial primary thinking have developed – I could say mutated – into a new strain.

"We have already seen the creation of a number of start-up companies that not only offer a practical backdrop to the academic work, but also promote the role of the institute to a new and fascinated audience. Trinity College, more than most, has pioneered this transfer of expertise.

"One of the guiding principles of my career has been the desire to promote the Irishness of my company and showcase the talents that this nation boasts. It is an enduring satisfaction to know that we, a tiny island nation, with hardly any indigenous resources outside of our own wit, can boast an exceptional educational pedigree.

"Ireland has evolved to the point where education and innovation have become prerequisites not only in terms of career progression, but in many cases survival. The introduction of new technology, such as genetic engineering and biotechnology, has unquestionably played a prominent role in advancing the development of this island nation. In the end, it is so much a matter of people, their education, their motivation, imagination and judgment. The Trinity geneticists have shown all of these qualities and played a major part in the emergence of biotechnology in Ireland.

"In today's highly competitive world, you either adapt or die. Personally, I believe that many of the companies which flounder are not in themselves unsustainable. What is unsustainable is the belief that good news is just around the corner. A personal saying of mine over the last four decades has been: 'Good news can always wait – manage the downside and the upside will look after itself.'

"Whether you wish to be the most successful packaging company in the world or the most highly-regarded learning institution, it is of fundamental importance that you adopt a

> A personal saying of mine is: good news can wait – manage the downside and the upside will look after itself

strategy that is consistent with your resources and your expectations. Sound businesspeople keep one eye on the present and the other on the future. I have learned through my contact with universities that it is the same for academics.

"For continued success, our highly-educated workforce and rapidly evolving technology sector need to be matched with enterprise in the fields of product development, research, design and innovation. And to achieve this we need our higher education to be of world-class quality.

"I know that the geneticists in Trinity have had to go through some very tough times and this has prepared them really well to take advantage of the new resources that are available for science in Ireland today, especially through Science Foundation Ireland."

Smurfit professor Seamus Martin

PROF SEAMUS Martin's work at the Institute of Genetics in TCD holds considerable promise for the development of new cancer therapies.

Martin, the Smurfit professor of medical genetics, along with his research team, has published a series of papers in leading international journals on the subject of programmed cell death. Recently featured in a *Nature Reviews* article, Martin's work examines how cells can commit suicide when injured or diseased.

The research also explores how and why cancerous cells resist being killed by drugs designed to eradicate them.

Martin's laboratory is ranked in the top 10 international research centres focused on cancer cell behaviour. His work has been awarded funding from Science Foundation Ireland (SFI). Martin completed his PhD research at NUI Maynooth in 1990.

He carried out his post-doctoral research in University College London Medical School, before going on to study HIV immunotherapy and tumour therapy at the La Jolla Institute for Allergy and Immunology in San Diego.

As well as securing SFI funding for his work, Martin has successfully applied for Wellcome Trust awards for a number of different projects.

Martin was awarded a full professorship at TCD in 1999. He is an expert on apoptosis, or programmed cell death.

As an SFI chief investigator, Martin and his colleagues in the Molecular Cell Biology Laboratory at TCD are using protein identification methods to chart alterations to cells undergoing apoptosis.

By understanding how cells normally behave during apoptosis, the research team hopes to uncover information which can be used to devise therapies aimed at manipulating apoptosis in disease situations. This has the potential to open up new methods to attack cancer cells and throw them into a natural "cell suicide" process.

– Louise Holden

A SPECIAL REPORT

TCDGeneticsat50

Sweet success of sugar beet research

The history of Trinity College Dublin's Department of Genetics is peppered with fortuitous incidents – not least the decision by the Irish Sugar Company to give funding for the support of the humble sugar beet, writes **Dick Ahlstrom**

> "Bacterial genetics was just coming on stream from the US, and Dawson must have been one of the first people to get involved – he was a pioneer in bacterial genetics

Left: David McConnell, Professor of Genetics at TCD. Photograph: Mac Innes Photography
Above: Prof George Dawson, founder of the department

THE HUMBLE sugar beet played a key role in the development of one of the world's most important genetics research groups. Interest in improving what was then one of Ireland's key crops helped Trinity College's new Department of Genetics at a pivotal time in its development.

The department has been ranked seventh in the world in terms of the number of references to research papers published by members of a university genetics department, says TCD's Professor of Genetics, David McConnell. This is despite the fact that the department has only been in place since 1958.

Ultimately, the creation of the department comes down to Prof George Dawson, a Cambridge graduate and research fellow who applied in 1949 for a vacancy in Dublin. Ironically, it wasn't in genetics at all but in botany, the subject in which Dawson had taken his BA.

His tutor had received a letter from David Webb, professor of botany at Trinity, indicating that a junior lectureship had opened up and asking whether there were suitable candidates about.

"George came over to Dublin in 1949, had a look and liked it and was offered the job. He moved over in 1950," says Prof McConnell. "He and Prof Webb taught the whole of botany at Trinity and George was an inspiring teacher."

But even as he lectured in botany, he pursued a different line of research. His special area of study while in Cambridge was bacterial mutations.

"Bacterial genetics was just coming on stream from the US, and Dawson must have been one of the first people in Britain to get involved," says McConnell. "He was a pioneer in bacterial genetics."

This was the time when researchers around the world sought to be the first to explain the mechanisms of inheritance. Dawson brought this research effort to Dublin and struggled to win funding. "Eventually, he got money from the old Medical Research Council of Ireland," McConnell says.

Dawson sent his research student, Stuart Glover, to one of the world's leading centres for this work, Cold Spring Harbor Laboratory in New York. The research goal was to map individual genes in the chromosomes. Dawson then sent another student, Edward Glanville, to Cold Spring. Later, Peter Smith-Keary took up the work in Dublin.

It was about this time, in 1953, that James Watson and Francis Crick made their Nobel Prize-winning discovery of the structure of the universal genetic code, DNA, the molecule used by every living thing to pass on genes to subsequent generations.

The study of genetics had reached a turning point and it grew rapidly. Happily, says McConnell, Dawson was a specialist in the field, which meant that Trinity would have an early entry to this groundbreaking science.

Money, as ever, was an issue, but then the common sugar beet made its contribution to the story. The sugar beet was one of Ireland's most important and valuable agricultural products at the time, and the head of the Irish Sugar Company, Lt Gen Michael Joseph Costello, decided that the country needed a breeding programme to improve the crop.

He learned of the genetics work under way at Trinity, and agreed with the university to provide £15,000 over three years to support teaching and research in fundamental genetics.

"The board decided to set up a department of genetics, and it was started in 1958." Who better to run it than George Dawson?

By then Dawson had been joined on the faculty by Peter Smith-Keary, but fortuitously the then government had decided to build up agricultural research, generally.

"An Foras Talúntais [the Agricultural Research Institute] was founded and Tom Walsh became its first head," McConnell says. "He was a visionary, and was assembling a team to set up agricultural research units all over Ireland. He appointed some brilliant young scientists."

Among them were Dr Vincent Connolly and Dr Patrick Cunningham, now the Government chief scientific adviser. "George persuaded the institute to allow these two young men to give lectures in the department," with Cunningham lecturing from 1962.

The first graduate from the young department of genetics in 1961 was Adrienne Jessop, who went on to complete a PhD. Other early graduates were Shahla Thompson and John Atkins, who together made a very important early discovery about how proteins are synthesised by genes.

Dawson and Smith-Keary became the "twin pillars" of the department, says McConnell, one providing a mathematical understanding of the genetic processes and the other specialising in the molecular biology of genetic inheritance.

Dawson became professor of genetics in 1967, the year after the current holder of that post, McConnell, finished his undergraduate degree in genetics. McConnell completed his PhD at the California Institute of Technology and then returned to Trinity College Dublin in 1970, where he has remained since.

"The department was still tiny back then," McConnell says. "There were only three students when I graduated."

By the mid-1980s, there were six members of staff – including Prof Peter Humphries, current head of the Department of Genetics – and staff and students were based in the former St Mark's Hospital.

"Then a great thing happened. Provost Bill Watts was trying to find benefactors who would endow professorships to celebrate the university's quatercentenary in 1992," says McConnell.

"Michael Smurfit agreed to endow a chair in medical genetics in 1989, and in 1990 Prof Stephen Whitehead was appointed. This was a tremendous fillip to the department."

New funders stepped forward, including the Wellcome Trust and the research charity that has long supported Humphries' work on the blinding disease, retinitis pigmentosa – Fighting Blindness.

By the mid-1990s, Provost Tom Mitchell was again in search of funding, this time because the then government had offered to pay half the cost of new research buildings being built on university campuses.

He suggested a replacement for the old St Mark's Hospital building and again received support, with a £2 million donation from Michael Smurfit, stg£2 million from Wellcome and funds from Chuck Feeney and Dr Martin Naughton (see page 2). The then taoiseach Bertie Ahern opened the new Smurfit Institute of Genetics in 1998. DNA's co-discoverer James Watson has been a frequent visitor to the institute, says McConnell.

He attended celebrations there in 2003 to mark the 50th anniversary of the discovery of the double helix, and is at Trinity this week as the Department of Genetics celebrates its 50th anniversary.

George Dawson, the man who started it all, retired in 1987, and died in 2004, aged 77. But his legacy continues to live on, helped in its small but significant way by the humble sugar beet.

Profile Science Foundation Ireland

"BIOTECHNOLOGY AND information and communications technology represent the engines of future growth in the global economy. A world-class research capability in selected niches of these two enabling technologies is an essential foundation for future growth."

So concluded the report commissioned by the Government in 1998, which led to the establishment of Science Foundation Ireland (SFI), a major supporter of genetics research at Trinity College Dublin. Established in 2003, SFI has responsibility for administering Ireland's Technology Foresight Fund.

"Out of our total budget of €12.3 million, Trinity has been a major recipient of funding," says Prof Frank Gannon, director general of SFI. "Ken Wolfe, for example, has received €1.3 million for investigations into yeast genetics (see page 6)."

SFI funding is awarded on foot of peer reviews of individual applications. Trinity is not a favoured institution; SFI is not pushing any one research centre over another, Gannon insists. Rather the quality of applications from key researchers at the institute is consistently high and getting higher.

"The Trinity Institute of Genetics is 50 years old, and is now in seventh place in the world in terms of genetics research. The standard of applications from Trinity gets higher every year, so it's no surprise that the institute is attracting so much funding from SFI."

As a selected niche of biotechnology research, genetics is becoming a recognised strength of the Irish research community. "In economic terms, such an outcome is obviously positive, but the work of the institute is not focused on commercial transfer," says Gannon. "This is high-quality research for the sake of knowledge and better understanding of the way genes work, for the good of human and animal health far into the future."

– Louise Holden

Passing on the genetic foresight to future generations

Whether laying the foundations for the discovery of DNA's structure or revolutionising bacterial genetics, Irish researchers have played key roles in the development of modern genetics, writes **Claire O'Connell**

IN 1953, James Watson and Francis Crick planted the American and British flags on a cornerstone discovery in genetics: the structure of the DNA helix. But Ireland and Irish researchers had a profound and recognised influence on the field in the lead up to that watershed moment, and they have run with the baton since, making world-class contributions to the practice and understanding of molecular genetics.

One of the most influential works of the pre-helical genetic era arose from a series of lectures delivered in Trinity in 1943 by physicist Erwin Schrödinger. Invited by Éamon de Valera to work in Ireland, the Austrian-born physicist turned his mind to the differences between living and non-living systems.

Nobody knew what a gene was, but Schrödinger guessed that genes had to have certain kinds of properties, they had to contain information and it was coded in some kind of molecular structure.

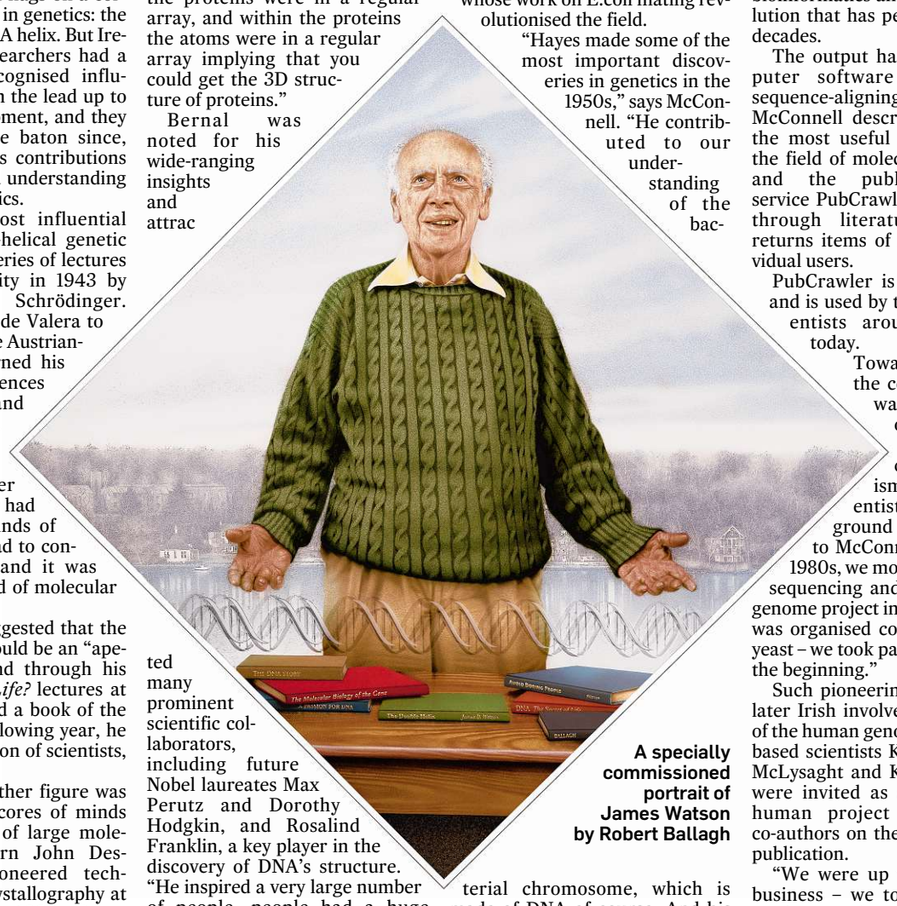
Schrödinger suggested that the genetic material could be an "aperiodic crystal", and through his seminal *What is Life?* lectures at Trinity in 1943 and a book of the same name the following year, he inspired a generation of scientists, including Watson.

Meanwhile, another figure was also influencing scores of minds about the nature of large molecules. Nenagh-born John Desmond Bernal pioneered techniques of X-ray crystallography at Cambridge in the 1930s, bombarding protein crystals with X-rays to generate scattered "diffraction" patterns.

"Bernal turned people's attention to the possibility that you may be able to find the structure of very large molecules like proteins, and he was aware that you could get crystals of purified proteins, including [the digestive enzyme] pepsin," says David McConnell, Professor of Genetics at Trinity.

"Bernal discovered a trick: if you suspend the protein in the liquid in which the crystal was formed, you could get these diffraction patterns. That indicated that the proteins were in a regular array, and within the proteins the atoms were in a regular array implying that you could get the 3D structure of proteins."

Bernal was noted for his wide-ranging insights and attrac



A specially commissioned portrait of James Watson by Robert Ballagh

ted many prominent scientific collaborators, including future Nobel laureates Max Perutz and Dorothy Hodgkin, and Rosalind Franklin, a key player in the discovery of DNA's structure. "He inspired a very large number of people, people had a huge respect for him," says McConnell. "This was the man who showed people that it was worthwhile trying to look at the structure of large proteins and molecules and indeed DNA."

Another mind that Bernal ignited was that of Maurice Wilkins, whose crystallography work helped uncover the stucture of DNA and earned him the Nobel Prize alongside Watson and Crick.

Although born in New Zealand and educated in England, Wilkins was genetically Irish, explains McConnell. "His mother and father were born in Ireland, and on his mother's side he was related to the great William Rowan Hamilton. Wilkins is 100 per cent Irish in his genes."

Apart from the race to work out the structure of DNA, other genetic research was continuing apace in the mid-20th century, and Rathfarnham-born physician Willam (Bill) Hayes was considered a leader in bacterial genetics whose work on E.coli mating revolutionised the field.

"Hayes made some of the most important discoveries in genetics in the 1950s," says McConnell. "He contributed to our understanding of the bacterial chromosome, which is made of DNA of course. And his work helped to establish that those chromosomes were made of circular molecules."

Trinity researchers John Atkins and Shahla Thompson also left their mark on bacterial genetics by discovering "recoding", where the base-pairs or "letters" of the genetic code are read in an unusual way.

"Pursuing the way the genetic code was sometimes read unconventionally led to interesting discoveries later, including that it is an important part in the way in which HIV is read out. It involves the ribosome occasionally reading four base pairs instead of three base pairs," explains McConnell.

McConnell himself spearheaded a move towards isolating stretches of DNA at Caltech in the late 1960s and came to Trinity in the 1970s, building up expertise in chopping out and sequencing stretches of genetic material.

Researchers here have since developed particular expertise in bioinformatics and molecular evolution that has persisted over the decades.

The output has included computer software such as the sequence-aligning Clustal, which McConnell describes as "one of the most useful programmes in the field of molecular evolution", and the publication-alerting service PubCrawler, which trawls through literature daily and returns items of interest to individual users.

PubCrawler is hosted at TCD and is used by thousands of scientists around the world today.

Towards the end of the century, the race was on to figure out the genetic sequence of complex organisms, and Irish scientists got in at the ground floor, according to McConnell. "In the late 1980s, we moved into genome sequencing and the first major genome project in the world which was organised co-operatively was yeast – we took part in that right at the beginning."

Such pioneering activity led to later Irish involvement in studies of the human genome, and Trinity-based scientists Ken Wolfe, Aoife McLysaght and Karsten Hokamp were invited as analysts on the human project and listed as co-authors on the landmark 2001 publication.

"We were up with this whole business – we took on bioinformatics, we became good DNA sequencers, good analysts and so we were involved at an early stage in these very big international projects," says McConnell.

"Broadly speaking, over the last 50 years, we have somehow managed to keep in touch over a time when the field of genetics was developing very fast, and whenever any new field emerged as important, we were either already there or we became involved in it reasonably quickly and always, I think, making decent contributions," McConnell says.

TCDGeneticsat50

A SPECIAL REPORT

Solid, sound investment in biotech

Ireland is an international giant when it comes to biotechnology – due to a combination of factors, including a strong regulatory system, an attractive corporate tax rate and, not least, a lasting link between top university research and industry, writes **Sandra Ryan**

Ireland's strong regulatory system is very important when producing drugs like Enbrel, for the treatment of rheumatoid arthritis (produced by Wyeth) or Gardasil, the vaccine to prevent the virus that causes cervical cancer (Merck and Co). Photograph: iStockphoto

IRELAND EMERGED from the bleak years of the 1970s and 1980s as the breeding ground for one of the fastest-growing biotechnology and pharmaceutical industries in the world. But who should get credit for this massive change?

Schering-Plough and Wyeth led the way by locating here in the 1960s and 1970s; the Government and Industrial Development Agency (IDA) Ireland (and, later, Science Foundation Ireland – SFI), determinedly planned the development; and universities, like Trinity College Dublin, were involved in the area from the beginning – when there was no funding – turning out high-quality science and medical graduates that are now vital to the industry.

Back in the 1970s, according to David McConnell, Professor of Genetics at TCD, the problem was not that there was no research being done, it was that they had no money or real support to do it.

"Trinity College has been involved in this since the beginning – in the 1970s, we were doing work here, studying genetics – with little or no support or funding, of course," he says.

"We eventually had companies like Biocon in Co Cork, a highly innovative company, supporting us. And it was companies like this that attracted more support for the biotechnology industry."

They also received great early support from the Guinness family, from Dr Tom Hardiman, and from Danish company Novo-Nordisk.

As awareness of biotechnology and genetic engineering and what it could do for people's health grew internationally, many people in Ireland took note and began lobbying for change, and for funding to make the changes.

In the late 1970s in the US, with the birth of synthetic human insulin, the biotechnology industry was growing rapidly.

Each new scientific advance captured the attention of both the media and the public, and by 1988, five proteins from genetically-engineered cells had been approved as drugs by the US Food and Drug Administration (FDA).

By the end of the 1990s, this number had jumped to more than 125.

"As the industry grew, the IDA began to become very involved, backing the whole idea of biotechnology and driving it forward in Ireland," says McConnell.

"Again, we already had places like Schering-Plough in Co Cork, which was one of the the first significant GM pharma plants in the world, and gradually, other companies were attracted here by the skill that was available and the research that was being done."

The IDA's strategy was vital to Ireland's growth, as was lobbying from the Irish BioIndustry Association (IBIA), part of the Irish Business and Employers Confederation (Ibec). According to Matt Moran, director of the IBIA – which was set up in 1996 to prompt government investment in biotech research – the fact that Ireland is now recognised as a hub for biotechnology is due to sustained planning from IDA Ireland, Science Foundation Ireland (SFI), and because of universities like Trinity College Dublin conducting high-quality research.

"Exports from the industry are now at about €43 billion, which is 45 per cent of our total exports," says Moran.

"There aren't many areas Ireland can 'major' in, but this is one. We have some big investors here like Wyeth, Schering-Plough, Pfizer, Eli Lilly, and also Genzyme and Centocor."

The list goes on, and includes Merck and Co, which has just got planning permission for a new €200 million site in Co Carlow, which will be a standalone vaccine plant, the first of its kind in the country. They will produce Gardasil, the vaccine used to prevent the virus that causes cervical cancer, Human Papilloma Virus (HPV).

"I think it's safe to say that, outside of North America, we have the highest amount of capital investment right now in this industry. We have managed to put ourselves in this position through sustained planning and investment," according to the head of pharmaceuticals and biotech at IDA Ireland, Barry O'Dowd.

The first major biotechnology investment in Ireland was Wyeth's, in Grange Castle in Clondalkin, Dublin 22.

Wyeth – which already had significant investment in Ireland at its pharmaceutical site in Newbridge – invested €1.8 billion in the project, which employs over 1,200 people, most of whom are educated to third-level degree or PhD level, and which produces Enbrel, a life-changing drug for rheumatoid arthritis sufferers.

Enbrel contains a genetically-engineered protein that blocks a natural substance in the body called tumour necrosis factor, or TNF, which is present in the joints of rheumatoid arthritis sufferers and activates cells that cause pain and inflammation. Enbrel works by disarming TNF.

Centocor Inc, meanwhile, a subsidiary of Johnson & Johnson, produces the drug Remicade at its plant in Ringaskiddy, Co Cork.

Remicade is used to treat autoimmune diseases such as rheumatoid arthritis, Crohn's disease, and psoriasis, and is highly successful, achieving sales of more than $1.3 billion (about €900 million) in 2003 – according to the company, it is the first biotechnology "blockbuster" to do so. So why are these industry giants settling in Ireland?

Barry O'Dowd says one reason is the the high quality of university research and scientific skill base.

"Trinity College is number two in the world for immunology citations,

> "Outside of North America, we have the highest amount of capital investment right now in the biotechnology industry

for example, and is recognised for its work in this area. It also ranks very highly for the quality of its work in genetics and has a very strong base in neuroscience — GlaxoSmithKline recently did a deal with the college, based on research being done into Alzheimer's disease. This link between industry and the universities is important," says O'Dowd.

Ireland's reputation for a strong regulatory system – very important when producing drugs – is also a deciding factor.

"If these companies are going to be making such big investments, they need to know they can get the product out quickly and properly, and to a high standard," says O'Dowd.

"Wyeth's rheumatoid arthritis drug, Enbrel, is a good example of this – that is, a €1 billion-plus drug, and needs to be produced in a good regulatory environment, which it is."

He listed Ireland's taxation rate as another reason – our corporate tax rate is 12.5 per cent; not the lowest, but still very competitive.

Perhaps the real way to judge how strong Ireland has become in the industry is to look at our reputation internationally – everyone agrees that people look at Ireland differently now, in the way in which the US was looked at in the 1960s and 1970s, and that it is now recognised as a hub of biotechnology. "If we go back to the 1980s, when what we had were heroic scientists doing the work with no funding, and compare it to nowadays, it paints an extraordinary picture," says Frank Gannon, director general of Science Foundation Ireland (SFI).

"TCD was a leading hub for this research, and became skilled at approaching the EU for funding – which meant the agenda was set by whatever the EU programme was at the time. Which obviously was not ideal.

"And now, R&D is not an add-on or a luxury, but a cornerstone of our economy.

"SFI came about because it was recognised that we needed to focus on science and on developing the industry. This was agreed on by everyone, including the then government and Mary Harney, then minister for Enterprise, Trade and Employment.

Frank Gannon, director general of Science Foundation Ireland

"The real master plan – and we have achieved this – was to move from a point where we just manufacture products, to one where we use the innovation and skill in this country to make, produce and research."

The next step, according to Matt Moran, is growing and developing indigenous companies out of the research being done here, and also developing the companies currently here and encouraging them to grow.

Pfizer, for example, now has its own internal bank in Ireland, and as biotechnology plants and products are developed, other, related companies follow – scientific software and device companies, for example. The future can only be bright.

Profile The IDA connection

THE INDUSTRIAL Development Agency (IDA) has been vital to the success of the biotechnology industry in Ireland. Its strategy for attracting business has paid off – Ireland now attracts 31 per cent of all healthcare investment coming into Europe and, in recent years, has had billions of euro invested by some of the world's biggest pharmaceutical and biotechnology firms.

According to Barry O'Dowd, head of pharmaceuticals and biotech in the IDA, it was joined-up thinking that led, in large part, to the area's growth. In 1958, Ireland introduced its first programme for economic expansion, which removed protectionism, encouraged foreign direct investment, and promoted exports. "The best evidence of the growth that has occurred is to look at some of the companies developing here – like Merck, which just got planning permission for a €200 million site in Carlow," says O'Dowd.

"Pfizer has just finished the validation process on their site in Dún Laoghaire – another huge investment, as is the Genzyme expansion in Waterford – there's an investment of €500 million in total. Centocor and Eli Lilly also have ongoing projects. I think it's safe to say that outside North America, we have the highest amount of capital investment right now in this industry."

How Ireland reached this position is due to a number of factors. "The quality of the graduates leaving the universities is important – most of the people needed to work in these developments are PhD-level graduates," says O'Dowd. "Another big reason we get the investment is that when companies are looking to invest, they are thinking of risk management and mitigation, from a corporate strategy point of view.

"They need to be sure they can build where the product will be delivered on time and to a high standard, and where their products will meet regulations. Ireland has an excellent regulatory system in place," he says. Ireland's favourable tax regime – with a corporate tax rate of just 12.5 per cent – is another point of attraction and we have a very strong science base. "Trinity College is number two in the world for immunology citations, for example, and is recognised for its work in this area. It also ranks very highly for the quality of its work in genetics and has a very strong base in neuroscience — GlaxoSmithKline recently did a deal with that department, based on work they are doing into Alzheimer's disease," says O'Dowd.

"The link with industry is important and I think Trinity's new biosciences building, due for 2010, will only strengthen this," he says.

– Sandra Ryan

Profile Professor Martina Newell-McGloughlin

ONE OF the leading experts on biotechnology in the United States is a woman who graduated in genetics from Trinity College in 1988, when she left the country – in which opportunities were then scarce – to pursue her career abroad.

Professor Martina Newell-McGloughlin directs the UC Systemwide Biotechnology Research and Education Programme (UCBREP). She won this programme away from UC Berkeley in 2001.

Her programme was singled out as an example of how a multi-campus research unit can reinvent itself to address evolving needs.

She is also co-director of a National Institute of Health (NIH) Training Grant in Biomolecular Technology, one of only four in California.

McGloughlin greatly contributed to the formation of Science Foundation Ireland (SFI) and is now a member of its board of directors. Her reputation in the field spreads further than just the US – the Vatican recently asked her to join a panel of distinguished scientists to brief them on biotechnology, or, as they put it, on the "opportunities and challenges" in the area. She will do this in May of next year, and remains admirably unaffected by her immense reputation as a scientist.

"The situation in Ireland was very different when I left the country – none of us could get jobs and a huge amount of people left," says McGloughlin, from her home in California.

TCD graduate, Prof Martina Newell-McGloughlin

"In the late 1980s, I left for the US and got a job as an assistant in the biotechnology department at UC Davis – it was a brand new job, exploring the whole idea of how to integrate the evolving biotechnology industry with academic research.

"I was basically working to integrate research being carried out in the industry with academic research – at that time, some academics looked down on the industry work as something you only did if you couldn't get involved in the academic side.

"When we first started integrating both fields, people in academia had no idea of the quality of the research being done by industry.

"There is now a dedicated emphasis on biotechnology research here, and in other universities – and in the National Institute of Health (NIH). So we've seen a huge change in a short period of time," she says. So has Ireland, and through her continued involvement with TCD and SFI, Prof McGloughlin has witnessed this change first-hand.

"I remember in the late 1990s, at the first meeting in Limerick that eventually led to the establishment of SFI, we agreed that the main priority in Ireland should be on promoting excellence in science. SFI really deserves a lot of credit for how much has changed," she says.

Also in 1999, McGloughlin met Mary Harney, then minister for Enterprise, Trade and Employment, when Harney visited San Francisco on a official visit.

"It was one of the best things I ever did, meeting her – I spoke to her and we listened to each other and I knew that if anyone could change Ireland, she could. That has worked – now people speak of Ireland as the place to go for research.

"People often ask me about Ireland, and many people are seriously considering it for research, the way they considered the US in the 1960s and 1970s," she says.

"I think there is more spent per capita on R&D in Ireland than currently in the US."

She still travels back and forth to Ireland, through her work with SFI and Trinity College, and continues to contribute to, and be proud of, the progress that has been made.

– Sandra Ryan

Realising the pharmaceutical potential Ireland has to offer

SANDRA RYAN

THE STORY of how Wyeth, one of the biggest investors in biotechnology and pharmaceuticals in the country, developed in Ireland is an interesting one. It highlights how the industry went from one in which people struggled to find employment – at a time when universities struggled for research funding – to one that now employs thousands and generates millions of euro in revenue.

Wyeth first came to Sligo in 1974 to produce SMA infant milk products. At that time, says Wyeth Biotech communications director Peter O'Brien: "People struggled to get jobs."

Over 30 years later, Wyeth runs a massive biotech plant, occupying 90 acres of land, at Grange Castle, in Clondalkin, Dublin – an investment of €1.8 billion that employs over 1,250 people and manufactures Enbrel, a treatment for rheumatoid arthritis and an excellent example of how genetic engineering can transform lives.

O'Brien explains why they chose Ireland to build the plant, which was opened by the Minister for Health, Mary Harney, in 2005.

"It really started with the drug Enbrel, which we jointly own with Amgen, an American biotechnology company. In 1999, because we wanted to manufacture the drug ourselves in Europe, we began looking at a number of locations," says O'Brien.

"The decision to invest in Ireland really came about because of a number of factors. One was tax reasons – Ireland had developed tax breaks for research and development [R&D] that are a huge advantage. Another reason was the quality of the people here – we needed about 1,250 qualified people who could build and operate the planned facility. Also we needed an adequate site.

"We found the 90 acres at Grange Castle in Dublin and it was basically ready for us – we could move in a week after planning permission was approved."

Of course, the fact that Wyeth already had successful plants in Ireland also helped – they set up their Wyeth Pharma division in Newbridge, Kildare in 1992, which was their first pharmaceutical investment in Ireland.

The Newbridge site – like the biotech plant – now has a co-located product development facility, and in total, the company now employs 3,300 people.

The Grange Castle site reveals some interesting statistics on employment in the industry. The average age of employees there is 33, and the ratio of male to female staff is approximately 50-50.

"These are young, highly-educated people; 65 per cent have a third-level degree, 5 per cent have a PhD and 15 per cent a Master's. And 30 per cent have a certificate or diploma," says O'Brien.

"Ninety per cent of employees came directly from Ireland, and of the 10 per cent we hired from overseas, 50 per cent were Irish people coming back to work here. In the late 1970s and 1980s, these people left Ireland for jobs – there were none here. This has obviously changed."

Wyeth runs a biotech plant, occupying 90 acres of land, at Grange Castle, in Clondalkin, Dublin, employing 1,250 people

The site has five plants: one for vaccines, two fill-and-finish plants for syringe and vials – where they manufacture and distribute prefilled syringes and drug vials – an Enbrel plant and a large development facility.

Four main products are developed on site – Enbrel; Prevenar, the pneumococcal vaccine; Tygacil, an antibiotic; and Relistor, a recently approved drug to treat the peripheral side effects of opioid use. "I think, to continue the progress and innovation, it is vital that science is continually funded in schools, at both secondary and third level," says O'Brien. "If we improve on the number of people doing science, we will ensure there are enough people in the area to do research and develop new medicines.

"We also need to keep making science fun and accessible for young people, so they stay interested in it. If not, there may not be enough people to work in the industry in years to come.

"And it is a fantastic industry to work in. You're coming to work knowing you are making medicines that will improve lives – it's a brilliant motivation," says O'Brien.

Timeline The growth of genetics at Trinity

1950
Bacterial genetics in botany
Bacterial geneticist George Dawson (ex Cambridge) appointed to Botany, Trinity.

1958
Department of genetics
Irish Sugar Company gives £15,000 to establish a department of genetics.

1959
Teaching in genetics
Dawson and Smith Keary start degree course and pursue bacterial genetics.

1964
Quantitative Genetics
(Trinity and Agricultural Institute) Patrick Cunningham (ex UCD, Cornell) and Vincent Connolly (ex UCD, Birmingham).

1970
Molecular Genetics
David McConnell (ex TCD and Caltech); first DNA sequencing (1976-7).

1975
Yeast Genetics
Bruce Carter (ex Edinburgh, Brandeis).

1975
Vincent Scholarships
Dr AWB Vincent founds scholarships to support summer research projects.

1979
Genetic Engineering and Biotechnology
Bustin, Ollington and McConnell clone the gene for amylase.

1982
Evolutionary Genetics
Paul Sharp (ex Edinburgh; now Edinburgh).

1983
Medical Molecular Genetics
Peter Humphries (ex TCD, Strasbourg).

1985
Human Molecular Genetic Mapping
RP Ireland Fighting Blindness funds a pilot project to map genes for retinitis pigmentosa.

1987
Plant Molecular Genetics
Tony Kavanagh (ex UCD, Cambridge) starts plant molecular genetics in Ireland.

1988
Genome Projects and Genome Evolution
McConnell joins European yeast genome project; Higgins (now UCD) and Sharp invent CLUSTAL (1988); Trinity in teams that sequence the whole genomes of yeast (1996), Bacillus subtilis (1997) and Arabadopsis (1999).

1989
Smurfit Chair of Medical Genetics
Steven Whitehead (ex Oxford, Harvard) appointed (1991); Seamus Martin appointed (1999).

1991
Clinical Molecular Genetics
(Trinity and St James's Hospital) Mark Lawler (ex TCD), Humphries and Sean McCann (St James's Hospital).

1992
Ocular Genetics Unit
Wellcome Trust funds the Ocular Genetics Unit.

1994
Neuropsychiatric Genetics
(Trinity and St James's) Michael Gill sets up Neuropsychiatric Genetics.

1994
Genetic Anthropology and Ancient DNA
Dan Bradley (ex Cambridge).

1995
Mouse Transgenetics and Gene Therapy
Humphries and Farrar.

1996
Human Genetics Degree

1998
Smurfit Institute of Genetics
Smurfit Institute of Genetics established with support from the EC, Atlantic Philanthropies, Dr Martin Naughton, Wellcome Trust and Dr Michael Smurfit.

2003
Double Helix
(Brian King) Donated by Dr Beate Schuler to commemorate the discovery of the double helix (1953).

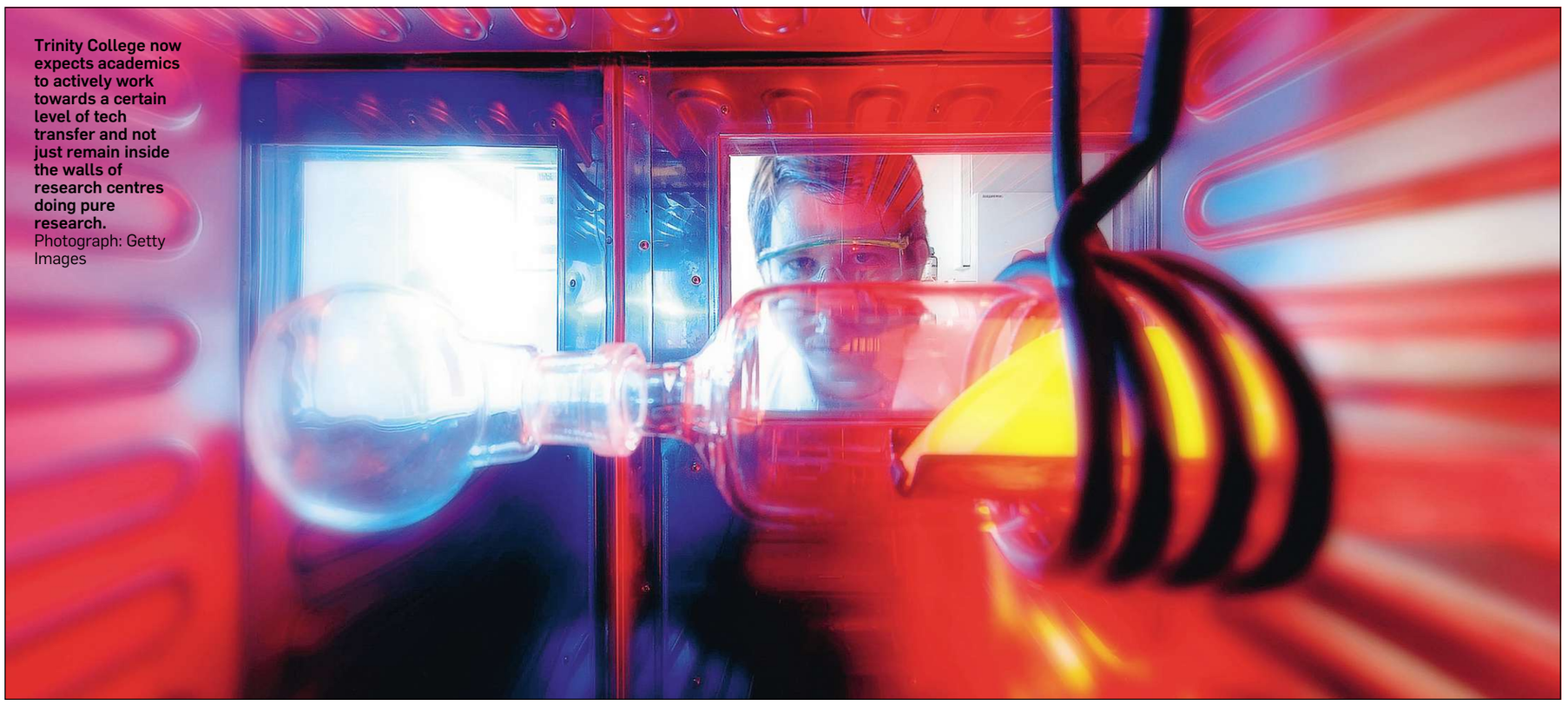
2002
Neurogenetics
Kevin Mitchell (ex TCD, Berkeley) (2002); Mani Ramaswami (ex Caltech, Arizona) (2006); Pablo Labrador (ex UC Berkeley 2006).

2006
Trinity College Dawson Prize in Genetics
First awardee: John Sulston.

2007
Epigenetics and oncogenetics
(Trinity and Tallaght Hospital) Adrian Bracken (ex UCD, TCD, Copenhagen).

A SPECIAL REPORT

TCDGeneticsat50



Trinity College now expects academics to actively work towards a certain level of tech transfer and not just remain inside the walls of research centres doing pure research. Photograph: Getty Images

Transfer of technology to the real world

Trinity College, with the support of Enterprise Ireland, is continually working towards making research more productive than research papers alone, writes **Karlin Lillington**

TOP-NOTCH research is always tough, but many academics find the greater challenge is to roll pure research over into a commercial application that can spin out a campus company.

In the past, figuring out how to make that transition easier and more successful – and identifying the research that has commercial potential in the first place – has been a major issue for third-level institutions as well as the Government agencies tasked with helping grow indigenous Irish businesses.

Meanwhile, the Government has also realised that commercialising research and creating businesses is not really a core strength of institutions focused on teaching and research, and that there needs to be more of a group effort.

To that end, Enterprise Ireland (EI) has established a programme to help fund expanded, dedicated technology transfer offices within third-level institutions to help transform groundbreaking, creative research into viable products, services or stand-alone companies.

At Trinity College, this new approach has meant an overhaul of the technology transfer process in Trinity's Research and Innovation office, says new associate director James Callaghan.

He's ready for a root-and-branch transformation, he says. "There are things we should be doing that we're not doing."

He also acknowledges that "the companies that have made it out so far have done so despite the system, rather than because of it".

In the past, tech transfer was a more casual affair, with a single person allotted to advise researchers and departments about getting laboratory work into the open market. Now, supported by EI funding, the office has five case workers, all with science PhDs and able to work with researchers through the entire patent and commercialisation process.

"Tech transfer is no longer just an administrative role, which makes all the difference with the academics," Callaghan says.

But he is clear that the process is also not one where academics might wander in on the off-chance that their research might have some commercial benefit.

Instead, he says that TCD now expects academics to actively work towards a certain level of tech transfer and not just remain inside the walls of research centres doing pure research, he says.

In part, that is because EI expects to see a rise in spin-offs and a growth in the intellectual property (IP) portfolio on the back of its funding of these new tech transfer offices, says Paul Roben, Enterprise Ireland's director for biotechnology in life sciences.

"The continued funding is dependent on further growth in tech transfer," he says. "We're putting funding in, in order to get results back out."

But those goals are matched by Callaghan's zeal to increase commercialisation from research.

"I want to build a culture where we're not afraid to spin out companies," he says.

"I also think we need to give a better return to the taxpayer than research papers alone."

In the past, TCD has spun out two to three companies a year, he says, and the intention is to increase this. "We should have companies going out every two to three months."

The infrastructure is already in place, to some degree – TCD's Pearse Street business incubation facilities are "the largest incubation centre in Europe", Callaghan says.

But he has a wide range of ideas on how to move commercialisation forward and make the whole system easier for academics.

He'd like to see some sweeping changes to the broader business and research picture in Ireland, for a start. He thinks that Science Foundation Ireland (SFI) focuses too strongly on large multinational involvement with research projects rather than on small, indigenous companies.

Bringing in smaller partners is of greater overall benefit to Ireland and Irish business, and would give support to young companies, many of them campus spin-outs, and create jobs within the country for Irish PhD students.

He also says there's a case to be made for "bundling or aggregating IP across the universities". This would merge complementary technologies and research IP, making for a stronger overall IP package.

As for what academics can expect, under the new system, a case worker is assigned to an academic or group to carefully go through the work they feel is patentable. If it looks promising, TCD will bring in finance and a management team for the company.

TCD takes a 15 per cent stake in the company for its involvement and because the IP was generated within its walls, Callaghan says.

Dr James Callaghan, associate director of TCD's Research and Innovation office

The issue of bringing in outside management is key, as often academics are not the right people to run a company, he says.

He is critical that in the past, academics have been expected to play both roles while maintaining teaching and administrative duties.

"Obviously there can be a very steep learning curve on the business side and those that cross over from academia into business can have a tough time," says Ronan Loftus, a TCD Department of Genetics academic who made that change himself to work as director of global commercial development for successful genetics research spin-off company, IdentiGEN.

Loftus is one of the rare academics who has made that shift, but most campus companies will need access to a potential management team, including entrepreneurial chief executives, and that is his office's role, says Callaghan.

He is hoping a growing number of TCD geneticists and other researchers will want to "give commercialisation a go."

"Innovation is a mindset, a culture, and you have to take time to build it and see if it works.

"I'm just trying to put different people and things together, and make new things happen."

Profile IdentiGEN: right time, right place for traceability

IDENTIGEN, A successful spin-off company from Trinity College Dublin's department of genetics, has, quite literally, created profit from the dust of old bones.

The company – which enables a single piece of meat to be traced back to its source – emerged out of genetic research at TCD into the genetic and evolutionary history of cattle breeds.

Using DNA that had been extracted from cattle bones, a research group, led by TCD geneticist Prof Patrick Cunningham – professor of animal genetics in the Department of Genetics at TCD and chief scientific adviser to the Government – found that cattle had been domesticated not just once in the early history of mankind, as previously believed, but twice.

DNA from ancient bones revealed two different branches for today's domesticated beasts, one that emerged in India and the other in the Middle East, about half a million years ago.

The research team soon realised that the same type of analysis they were using could give a cut of beef or a piece of chicken in a shop or restaurant perfect traceability. It would provide a way of linking the meat back to the animal or farm from which it originated.

With increasing concerns about food safety and origins in recent years, IdentiGEN and its simple and inexpensive test for confirming meat origin was the right idea, in the right place and, crucially, at the right time.

Ronan Loftus, IdentiGEN's director of global commercial development and a Trinity genetics graduate who has moved into business, says that the company owes much of its origins to TCD.

"Within the department of genetics, there was a very favourable environment and strong encouragement," he says.

The young company benefited enormously from having access to the college's laboratory facilities to start with – for a young start-up like IdentiGEN, the sheer cost of setting up such labs on their own would have been a significant stumbling block to the viability of their business plan, says Loftus.

Loftus also believes that the constant contact with other academics at TCD, and access to research students have been a huge help to the company. Having solid academic research behind the company and founders with published research "was helpful and lent credibility" to their enterprise, he says.

"We recently have established a facility in the US and we draw on the science and the association with TCD for that centre, and also for special projects," says Loftus.

He also points out that most venture capital firms "take comfort in the fact that the technology is derived from a sound academic background" when considering making an investment.

IdentiGEN has already achieved some international prominence. Its DNA "TraceBack" technology was used by the BBC *Panorama* programme to show that Dutch chicken producers were injecting water and proteins from pork and cattle into chicken meat to plump it up.

From its US base in Kansas – in the heart of US cattle country – IdentiGEN hopes to expand even further in the services it provides around the world.

– Karlin Lillington

Protecting good ideas before they become public property

Unique processes are being discovered daily by researchers – and protecting them through the patenting process is critical, writes **Karlin Lillington**

Once an Irish patent has been issued, researchers can then approach the European Patent Office (above). Photograph: iStockphoto

WHEN IT comes to patenting – protecting the intellectual property produced by researchers – the academic drive to publish and present at conferences can be a researcher's downfall.

"You can only patent something if it hasn't been made public," warns Dr Siobhan Yeats, director of the biotechnology directorate at the European Patent Office (EPO).

Many academics have made the mistake of speaking about or publishing their work before protecting it, enabling someone else to sneak in and file a patent ahead of them.

With a doctorate in genetics from Trinity College, Yeats is well positioned to understand the complexities facing researchers when filing for patents.

"Researchers should start by talking to their technology transfer offices about their work, to see if there is work that should be protected," she says.

Dr James Callaghan, associate director of Trinity Research and Innovation, agrees.

"I want academics to think: 'Is there anything that can be patented?' We're here to facilitate the technology transfer," he says.

With several case workers – all with PhDs themselves – ready to help, researchers at TCD can be linked up with patent attorneys who begin the process of protecting intellectual property.

Patent attorneys are different from regular attorneys in that they bring a science background and bridge the worlds of science and law, says Yeats.

The first place they will go is the Irish patent office, as a patent should first be applied for in a researcher's home region, she says. The office can also offer advice and help to those starting out on the process, which can be quite involved.

"Essentially, when a researcher in academia or a company has an idea, that's when they contact us," says Anna Hally, patent attorney with Dublin firm Cruickshanks and another TCD genetics graduate. At an initial meeting, the attorney discusses what patent attorneys call "the invention", the unique process the researcher hopes to patent.

Most researchers tend to be working on a very narrow aspect of an invention within academia, and for patenting purposes, need to broaden out. "We want to patent a general concept," Hally says.

A patent specification is a specific technical and legal description that needs to be slightly different for different territories, too – so a fresh specification is used for Ireland, the UK or the EU.

Genetics applications have their own sets of challenges, Hally notes. "With biotechnology, it's a very young technology and patent law was written before it was invented. It takes a while for law to catch up with technology," says Hally. Therefore, it is particularly important for patent specifications to be watertight as there's a good chance they will be scrutinised in court as legal cases are actually what define much of this new patenting area.

Once an Irish patent has been issued, researchers can go to the EPO to get European-wide protection for their intellectual property. This requires a validation process to verify the work patentable, says Hally. Once granted, the patent will be valid in any of 32 countries, though recognition of the patent must be filed for in each state's patent office.

Filing in the US is a separate process, somewhat different from the European process, and is advisable for many researchers.

The number of Irish patent applications is still small, says Yeats, though it is increasing. The bulk of patents filed for through her division come from the US, with the UK and Germany the largest European applicants.

These days, with the boom in life sciences research, her department is kept busy. They have over 260 people working on biotechnology patents in her office.

"Twenty years ago, we had maybe 10 people working in the area. The field exploded in the 1990s," she says.

She has worked in the EPO during exciting biotechnology times, when the human genome was decoded. Her work brings her in contact with Nobel prizewinners who, she says, tend to be very good at explaining their projects when applying for patents.

Her advice to Irish researchers?

"They should go at the matter with a more open mind about the potential of their work," she says. "They should think about what could be patented."

TCDGeneticsat50

A SPECIAL REPORT

TCD genetics graduates make a far-reaching impression

Graduates of TCD's Department of Genetics have made an impact internationally. Photograph: Mac Innes Photography

PETER McGUIRE

GENERATIONS OF Trinity College genetics graduates have made a major impact on the world. Australia, the US, England, Scotland, and India are among the many countries in which TCD genetics alumni are engaged in ground-breaking research.

Some graduates, like Dr Mittur Jagadish, were drawn to TCD due to its reputation. Jagadish, now director of Monsanto Research Centre in Bangalore, left India in 1976 to undertake his PhD.

"Dublin is etched in my memory," he says. "The broad-mindedness of Prof George Dawson [former head of genetics], and the excellent mentoring skills of my supervisor Dr Bruce Carter, were a major factor for me."

To date, Jagadish has influenced various fields of genetics, working at the Waksman Institute of Microbiology, Rutgers University, New Jersey, and later at the Boyce Thompson Institute for Plant Research at Cornell University in New York.

Jagadish also spent 11 years at the Division of Biomolecular Engineering in Melbourne, Australia, where he was a leading member of the team responsible for producing a genetically-engineered sub-unit vaccine against a viral disease in poultry, for developing a plant virus-based vaccine presentation system, and establishing different expression systems to synthesise recombinant proteins.

Prof John Atkins works at the BioSciences Institute of University College Cork and the Department of Human Genetics at University of Utah. He says: "As an undergraduate, I was struck by a lecture by George Dawson, so I switched from agriculture to science."

Atkins entered a research career that has focused on seeking and later studying, cases where the genetic code is read out by locally altered rules in response to programmes built into the coding sequence. He explains: "The meaning of a code 'word' can be dynamically changed, the reading register altered or a block of coding sequence bypassed, resulting in the synthesis of extra or enhanced proteins or regulatory consequences. Arising out of this work has been a deep interest in RNA, similar to DNA, which it likely predates. Recent work has shown RNA plays a much larger role in all living organisms than anyone imagined, as can be seen in *The RNA World*, freely downloadable at rna.cshl.edu."

Prof Georgia Chenevix-Trench **(see panel, right)**, who is carrying out ground-breaking research aimed at the discovery of novel breast cancer genes at the Queensland Institute of Medical Research (QIMR) in Australia, graduated from TCD in 1980. QIMR, home to over 700 scientists, is one of the largest medical research centres in the southern hemisphere.

In 1996, Chenevix-Trench became involved in a national consortium to study all aspects of familial breast cancer. She has now been joined at QIMR by two further TCD genetics alumni, Brian McEvoy and Enda Byrne.

Thousands of miles away, Andrew Grimson is a postdoctoral fellow at the Bartel Lab in the Whitehead Institute at the prestigious Massachusetts Institute of Technology (MIT).

He is grateful for the doors TCD opened for him: "From the start, the genetics department stood out – people always seemed to enjoy what they were doing. The lecturers frequently conveyed the idea that genetics was about learning how to learn new things – far more interesting than simply presenting facts to be memorised."

Grimson's most significant opportunity was the chance to join the Atkins/Gesteland lab in Salt Lake City. He is currently working on microRNAs, a new class of regulatory molecules, which contribute to the regulation of about half of mammalian genes.

Closer to home, Stephen Bustin is a Professor at Barts and the London School of Medicine and Dentistry, the medical faculty of Queen Mary, University of London. He has been heavily involved in the polymerase chain reaction, which can be modified to perform genetic manipulations, and has published the most widely-cited review on this subject. His main scientific interests revolve around bowel diseases, and he sits on the boards of several journals.

"My main memories of the department are of the friendly and supportive atmosphere, the fabulous support offered by the technical staff, and the outstanding vision provided by Prof David McConnell, which has served as my inspiration ever since," he says. "David represents the dynamism, promise and humanity of genetics, which have stayed with me to this day."

Profile Prof Georgia Chenevix-Trench

"I CAN pinpoint the exact moment when I decided to become a geneticist. It was at the lunch for new Scholars and Fellows in May 1978, when Prof David McConnell invited me to see him the next day. When I graduated from the genetics department in 1980, I knew I wanted to move into the area of human genetics, but the field was poorly developed in Ireland at that time.

"McConnell suggested I write to the 'grandfather of human genetics', Victor McKusick, for advice. McKusick recommended that I apply to the Medical College of Virginia, a decision supported by Mike Conneally, a well-known Irish geneticist in Indiana. I did my PhD in Virginia during the time that many of the genes for hereditary diseases were identified, and when the field of human cancer genetics was born, with the discovery of tumour suppressor genes and oncogenes. I then married an Australian geneticist, Nick Martin, and moved to Brisbane in 1986.

"At first I dabbled in various aspects of genetics, but in 1996 we started a national consortium to study all aspects of familial breast cancer. This consortium is now the best in the world for this purpose.

"I am particularly interested in the discovery of novel breast cancer genes, and for the past three years have been working intensively with researchers from all over the world. Some of this work was published last year in *Nature*, the premier science journal. I have always been funded to do pure research and climbed steadily up the ladder to a professorship in 2007.

"Nick and I were the first geneticists, and the first non-Queenslanders, to be appointed to our institute, the Queensland Institute of Medical Research (QIMR), in 1988. QIMR is now regarded as the best centre of genetics research in Australia, and has attracted several excellent people from TCD. Brian McEvoy and Enda Byrne are here now, and Byrne did some of his prior training with Mike Conneally, so the Irish links remain very strong. We wish we could be there for the birthday party this week.

– Louise Holden

A glance at the detailed history of evolution

Bioinformatics is involved in almost all areas of genetics – exploring ideas and analysing the results of experiments with a previously unknown level of accuracy, writes **Karlin Lillington**

EVOLUTION USED to be about bones and fossils, but it's now more likely to be about molecules and computer programs.

Instead of the giant dinosaur skeleton defining the endless human search to understand how creatures have evolved over time, scientists now examine molecular structure to peer into the a detailed story of evolution with an accuracy that Charles Darwin could hardly have imagined.

This is the field of molecular evolution, the study of how genes have evolved and why genomes – the compete set of genes in an organism – are organised the way they are.

Molecular evolution is closely linked to the field of bioinformatics, which involves the use and development of computer methods to analyse the vast quantities of DNA data now available.

Without bioinformatics, molecular evolutionists could not productively examine and compare the molecular building blocks of DNA and other structures, the basis of molecular research.

Almost all areas of genetics research now involve bioinformatics, either as a way of exploring ideas for further lab research, or in order to handle the results of large-scale experiments.

And though these areas of study may sound esoteric, they have surprisingly practical applications – from better understanding why a racehorse runs well, to learning how to create medicines that are better at targeting specific diseases, to medical forensics.

In the latter case, molecular evolution has been used in court cases – for example, to determine whether a person could be held responsible for deliberately infecting another with HIV. Molecular evolution can reveal when an infection occurred.

> "The genomics revolution has showered us with data – the information revolution has given us the ability to analyse it as a whole," he says.

Trinity College Dublin's genetics department produces strong research in both of these fields.

Dr Paul Sharpe, originally at TCD but now at the University of Nottingham, is credited with launching the field in Ireland, and his molecular analysis of viruses has contributed to understanding the origins and evolution of the Aids virus, which in turn has helped researchers work towards more effective ways to battle it.

Within TCD today, cutting-edge work is done by researcher Prof Ken Wolfewithin the Smurfit Institute. Wolfe's work focuses on understanding the evolution of yeast, and gene doubling – a process that can indicate the branching off of a new species, thus giving insight into the evolution of a species.

Wolfe has written of his field: "For molecular evolution researchers, the genomics revolution has showered us with raw data and the information revolution has given us the wherewithal to analyse it.

Prof Ken Wolfe from Trinity College Dublin's Department of Genetics, whose work focuses on understanding the evolution of yeast, and gene doubling – which can indicate the branching off of a new species, giving insight into its evolution. Photograph: Aidan Crawley

"In broad terms, the most significant outcome of these changes has been our new-found ability to examine the evolution of genomes as a whole," he says.

He has also, with TCD genetics colleague Karsten Hokamp, created a webcrawler program called PubCrawler that has benefited countless researchers by finding all new publications online in the scientific field of one's choosing.

Given the frequency of publication in many areas, the programme – used by over 40,000 researchers – makes staying abreast of the latest work in a field far easier and saves hours of online research time.

Another molecular evolutionist working in intriguing new areas is Prof Dan Bradley, whose work has helped unveil the origin of domestic cattle by examining ancient DNA from cattle – and also looking at DNA from the extinct Great Irish Elk.

Many know him better for his work in revealing some of the origins of the people of Ireland, again from molecular analysis of DNA.

Dr Aoife McLysaght of the Smurfit Institute Molecular Evolution Lab is looking at the origin and evolution of genes and gene loss in invertebrates and viruses.

Molecular work also contributes to the field of medicine. At TCD, Dr Andrew LLoyd is exploring the evolution of the human immune system.

Trinity researchers in molecular evolution and informatics are also placed at other institutions where they contribute to a wide range of research.

One such researcher is Emmeline Hill, originally at the Smurfit Institute and now at University College Dublin's Department of Animal Science and Conway Institute.

From a family with a horse breeding background, she is comparing gene-expression profiles from horses when exercising and when relaxing to better understand what makes some racehorses better than others.

But such research may well have a wider impact, offering insight eventually into human athletic performance or health problems like obesity.

Former TCD researchers Des Higgins, Denis Shields and David MacHugh are also pursuing research at TCD.

Recognition of extraordinary and original research

Ground-breaking research should always be recognised, which is the aim of Science Foundation Ireland's President of Ireland Young Researcher Awards. Below are two recent recipients of the awards at Trinity College

DR AOIFE McLYSAGHT

In 1998, Dr Aoife McLysaght graduated from Trinity College Dublin with a first-class honours degree in genetics.

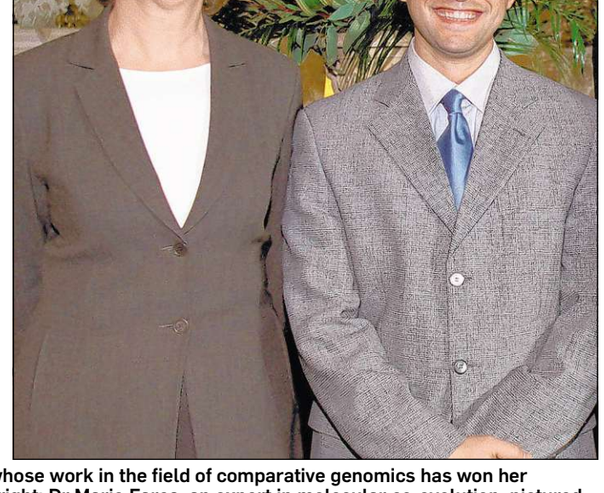
Following the completion of her PhD, McLysaght moved to southern California to work as a postdoctoral researcher with Prof Brandon S Gaut.

In 2003, McLysaght took up a lectureship in genetics at Trinity College Dublin. She established her own research group in the field of comparative genomics and lectures in evolutionary genetics to undergraduate students.

McLysaght's research has won her international recognition. She has been invited to speak at international conferences, to conduct peer reviews for leading international journals and was associate editor of the journal *Molecular Biology and Evolution*.

McLysaght is now leading research into the evolution of genomes.

Her investigations are designed to uncover aspects of the evolution of genes, leading to a better understanding of how genes operate.



Above left: Dr Aoife McLysaght whose work in the field of comparative genomics has won her international recognition. Above right: Dr Mario Fares, an expert in molecular co-evolution, pictured with President Mary McAleese. Both received SFI President of Ireland Young Researcher Awards

DR MARIO FARES

After completing his studies in the University of Valencia, Dr Mario Fares graduated with a degree in biology 1997, with special focus in genetics and statistics.

He completed his masters thesis in the molecular dynamics of the foot-and-mouth virus. In July 1998, he was awarded the Extraordinary Prize for his academic achievements by the University of Valencia. The subject of his PhD was the the role of heat-shock proteins in the maintenance of bacterial endosymbiosis using bioinformatic and molecular techniques.

During his postgraduate studies, he also studied in the Department of Zoology in Oxford University, researching the evolution of RNA viruses. In 2002, Fares accepted a postdoctoral position in bioinformatics with Prof Ken Wolfe in the Department of Genetics at Trinity College Dublin.

In 2003, he took up a permanent lectureship in the Department of Biology at the National University of Ireland, Maynooth.

Fares' publication record covers his various fields of expertise including articles in *Nature* and the *Journal of Molecular Evolution and Bioinformatics*.

He has fostered collaborations with leading research groups in Oxford and Spain, and plans to build new partnerships with both biomedical and bioinformatics teams around the world.

Fares is developing multidisciplinary computational biomedicine research, by training postgraduate students and developing course material, bridging these two vital areas.

Profile Prof George Dawson

PROF GEORGE Dawson (1927-2004) made many exceptional contributions to Trinity College in the fields of art and science.

A graduate of Cambridge University, Dawson joined Trinity School of Botany in 1950 and continued his work on bacterial genetics.

In 1958, he convinced the Irish Sugar Company to award £15,000 to the university in order to establish the Department of Genetics. In 1960, it produced its first graduate, Adrienne Jessop.

Dawson, with the Trinity Agricultural Institute and two of its researchers, Paddy Cunningham and Vincent Connolly, gave courses in plant and animal genetics.

He provided extraordinary leadership at the genetics department for 30 years, ushering in new styles of teaching and assessment. He placed great emphasis on evidence, and his pedagogical philosophy informs the work of the institute to this day.

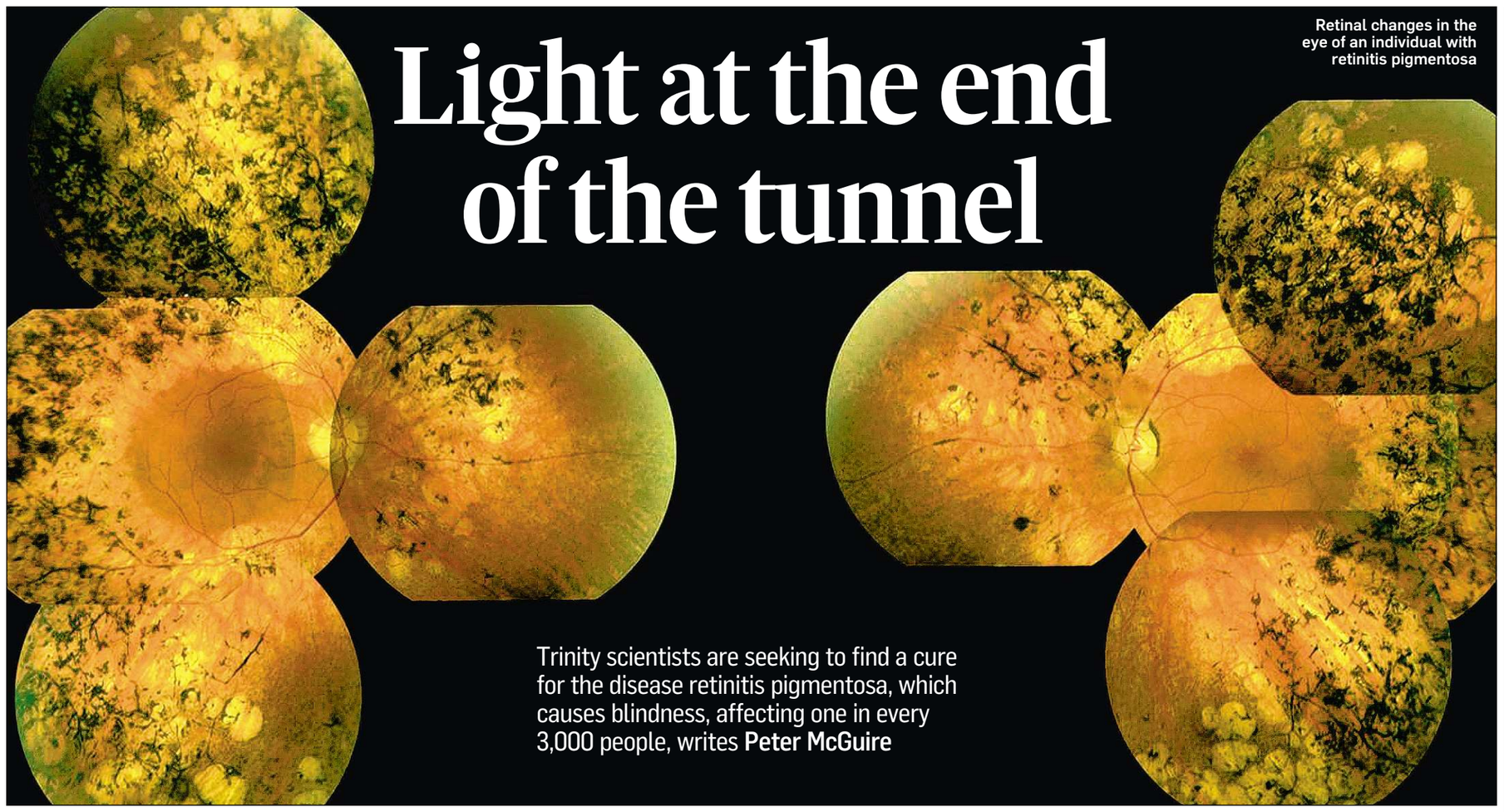
Dawson placed mathematical and molecular study at the centre of genetics research. He was very supportive of students and instilled in them the sense of excitement that scientific discovery can engender. He nurtured talent, and tried to create as many opportunities for his students as he could.

The Institute of Genetics is his legacy to Trinity College. He was also instrumental in the establishment of the Douglas Hyde Gallery, and the Department of History of Art. Dawson left a lasting mark on Trinity, and played a seminal part in building its current international status in genetics research. *– Louise Holden*

■ The painting of George Dawson above, by Mick O'Dea hangs in the Smurfit Institute of Genetics at Trinity College

A SPECIAL REPORT

TCDGeneticsat50



Light at the end of the tunnel

Retinal changes in the eye of an individual with retinitis pigmentosa

Trinity scientists are seeking to find a cure for the disease retinitis pigmentosa, which causes blindness, affecting one in every 3,000 people, writes **Peter McGuire**

IT OFTEN begins with a loss of night sight. Gradually, over a number of years, the field of vision narrows until, for most sufferers, they can see only a small chink of light at the end of a tunnel.

Retinitis pigmentosa (RP) – which leads to tunnel vision – is one of the most common forms of inherited blindness, affecting approximately one in every 3,000 people. It is a debilitating, progressively degenerative disease that robs people of much of their sight.

But, for the many millions affected, a breakthrough comes closer by the day. Since 1985, a dedicated research team at Trinity College's Smurfit Institute of Genetics has been working towards an eventual cure for RP.

Dr Jane Farrar and Prof Pete Humphreys, working with clinical ophthalmology surgeon Dr Paul Kenna – who is central to the project – head up the team of over 20 people at TCD. Their work has led them through large-scale family genetic research to genetic mapping, and now, towards an effective cure for this debilitating condition.

"The project began through the efforts of Michael Griffith of Fighting Blindness," Farrar recalls. "They approached the Department of Genetics to carry out research on the disease. When I began this as a PhD student, I was tracing Irish families with RP. In particular, I was looking for large families; bigger families have a bigger gene pool and more opportunities for research."

Farrar, Humphreys and Kenna's team worked with the gene that codes for rhodopsin, a protein at the back of the retina which absorbs light, turning it into electric signals and, ultimately, allowing us to see. In some people, however, a mutation in this gene damages rhodopsin.

> "The primary goal is to develop safe and effective therapies for people who are losing their vision

Now the team know that there are at least 40 genes involved in the various forms of RP. The next step, according to Farrar, involves designing gene therapies to treat the condition. These can be delivered by harmless viruses, which have proven themselves as nature's most effective cell invader. "There are many hugely modified viruses that have no associated toxicity – Trojan horses for delivering genes to a cell. These are really well tolerated by the human eye."

The team hope to begin human clinical trials within the next few years. Already, Farrar and Humphreys have carried out research with specially bred, genetically modified mice.

Mice lacking rhodopsin have developed sight after being injected with a healthy copy of the relevant gene, whereas mice injected with the mutant gene do not.

Last year, doctors at Moorfield's Eye Hospital in London carried out clinical trials with three volunteers suffering from Leber's congenital amaurosis, a condition which leaves most patients completely blind by their late twenties. The doctors injected a harmless virus with a healthy copy of the RPE65 gene into the patient's retina. One of the volunteers enjoyed significantly better vision, but the others have yet to show any sign of improvement.

"We are working on a few forms of RP," Farrar says. "Depending on what genetic technologies arise in the next few years, this research could outlive me entirely.

"The primary goal is to develop safe and effective therapies for people who are losing their vision," Farrar concludes. "The team is working on more than just RP. We are also interested in age-related macular degeneration, which affects one in 10 people over the age of 65.

"This is where the cones, which are involved in day and functional vision, begin to degenerate. Ideally, we would like to expand our work programme so we are not just involved in the debilitating disorder RP; we also want to look at common forms of blindness and develop safe and effective therapies for debilitating disorders."

Above: Dr Jane Farrar and below: Prof Peter Humphreys, head of the Department of Genetics at TCD

Case study Quest for a cure

THE IRISH quest to cure retinitis pigmentosa (RP) began in 1983, when a small group of people met in a little hotel on Gardiner Street in Dublin.

From this meeting, Michael Griffith **(pictured right)**, whose father suffered from RP, set up Fighting Blindness. Later, Griffith would himself develop this genetic condition.

"I attended a meeting of Retina International in Helsinki, where I came across the first breakthrough in RP genetic research," Griffith recalls.

"I was hugely enthused. We approached the Department of Genetics in Trinity, and it wasn't long before research was up and running," he says.

Fighting Blindness has proven to be a particularly effective fundraiser, providing vital money for Trinity's researchers to conduct their work. Over the years, the two organisations have worked closely with one another, each bringing new and fresh approaches to the problem of RP.

"The Fighting Blindness story is one I hope might give encouragement and hope to other people," says Griffith.

"If the therapy is developed and put on the market, it would be a fairytale story.

"We were just a scrawny bunch of people in a hotel room, but I hope we have shown that you can fight these things and that there are solutions," says Griffith.

"These things take time, but if we get there in the end, it will all have been worthwhile," he says.

A forensics team seek evidence at a crime scene – DNA evidence is often a part of the prosecution's case

The star witness for the prosecution

CLAIRE O'CONNELL

FEW ASPECTS of DNA analysis have captivated popular attention as widely as forensics.

Television programmes like *CSI* and high-profile court cases highlight the trials and tribulations of using DNA to help solve crimes. and genetics is a rapidly developing component of the Forensic Science Laboratory at An Garda Síochána Headquarters in Dublin's Phoenix Park.

A day's work in the DNA section involves extracting and examining genetic material that can shed light on crimes, according to Dr Louise McKenna, the laboratory's deputy director.

"It's about analysing samples from scenes of a crime and comparing them with samples from victims or suspects. So we are talking about murders, sexual assaults, armed robberies – quite a range of crimes," she says.

The samples can be of bodily fluids or may contain cells from skin or the roots of hairs, explains McKenna. As a result the careful removal of samples from a scene is critical.

"If you are hoping to find DNA that has been left by an offender, you target the areas that they have been in contact with and where there's unlikely to be too much DNA from other people," she says.

"If you have a strangulation, you may target the neck area and if it was done with bare hands, you may have foreign DNA there and you might pick up that. You are very dependent on the scenes-of-crime people who are looking at the place and seeing what is likely to yield evidence," says McKenna.

Minute amounts of DNA extracted in the lab from the collected samples can be scaled up using a technique called polymerase chain reaction (PCR), a type of molecular photocopying that generates enough DNA to determine its sequence.

The scientists zone in on up to 10 areas of "nonsense" DNA that offer good variation for discriminating between individual people, explains McKenna. The resulting profile carries a risk of less than one in 1,000 million of an "adventitious" or innocent match with other, unrelated people.

"When we are reporting we will always say the frequency of the match but there won't be a discrimination between close relatives, siblings, children or parents," says McKenna.

Even where there's no close genetic relationship to contend with, there can be other difficulties with sourcing samples.

"If you take the case of Joe O'Reilly, who was convicted of murdering his wife, he was living with her, so DNA really couldn't help there. People were saying 'well you should be able to find foreign DNA there', but the trouble is that most DNA on surfaces is mixed DNA, and once you get beyond a mixture of two people you can't interpret it."

However, when DNA is a useful option, it can help solve a criminal case, says McKenna, particularly in countries with a national DNA database.

"That's where there is legislation that allows the police to take samples from people who have committed crimes or have been suspected of committing crimes, and those samples are put on a database and usually kept for a long period of time," she says.

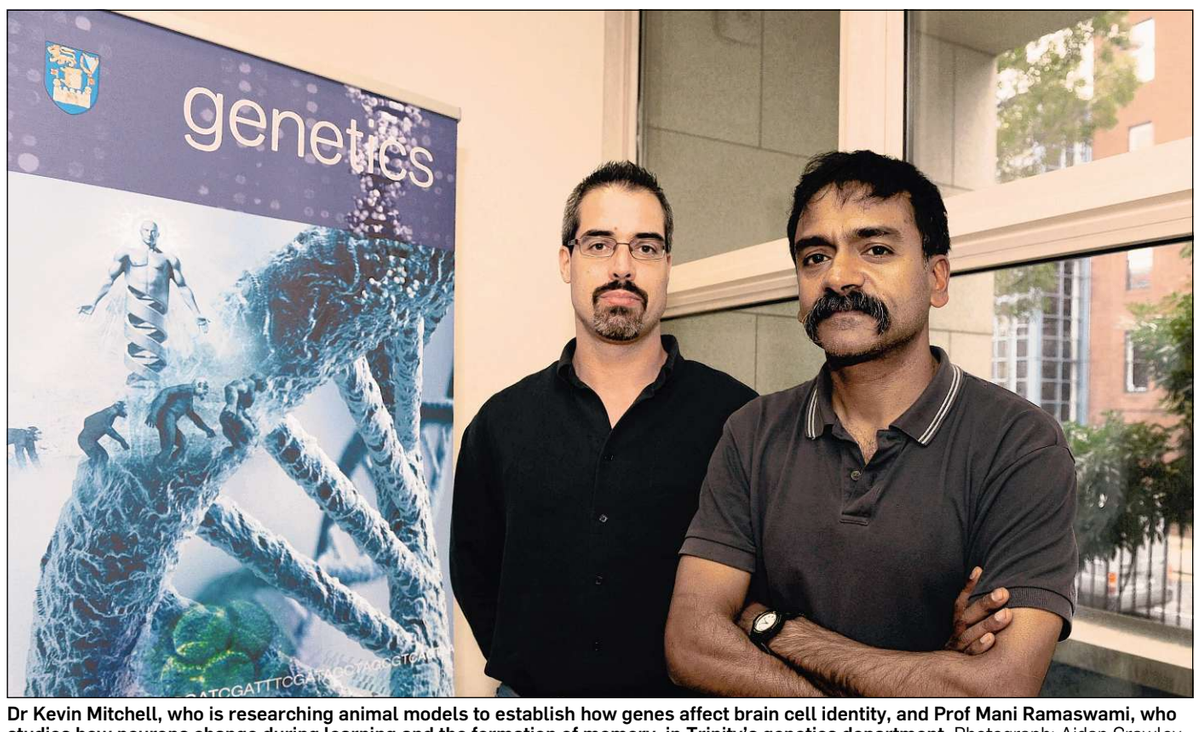
"So any other crimes where DNA may have been left behind can be checked against the database. This has solved an awful lot of crimes in other countries. And it has been talked about [in Ireland] for quite a while, but it hasn't happened yet."

McKenna notes that the lab in the Phoenix Park has had a working relationship with Trinity since before the forensic DNA service was started in 1994.

"When we began to realise that DNA was a technique we wanted to develop, we decided to send one of our scientists to learn the techniques in a laboratory before we learned the forensic applications of the technology, and a scientist went and spent a few months in one of the research labs in Trinity in the early 1990s," says McKenna.

'Neurogenetics has not yet broken as a subject' – but the result will surely be worth the wait

Trinity researchers are at the forefront of developments in the area of neurogenetics, beating a path to the maze of unknowns that is the human brain, writes **Claire O'Connell**



Dr Kevin Mitchell, who is researching animal models to establish how genes affect brain cell identity, and Prof Mani Ramaswami, who studies how neurons change during learning and the formation of memory, in Trinity's genetics department. Photograph: Aidan Crawley

TRINITY COLLEGE Dublin (TCD)'s genetics department has chalked up an impressive research output in its 50 years to date. But at a time when our understanding of the molecular workings of the cell is advancing rapidly, what's next?

One of the hottest areas of development is in neurogenetics, or how DNA underpins the wiring and function of our brains.

"There are really exciting things in all aspects of genetics, but I think a lot of people would say that neurogenetics has not yet broken as a subject," says David McConnell, Professor of Genetics at TCD. "It is one of the great black boxes – we don't understand how the brain works. We know it's an electrochemical machine, but there is so much to learn about it."

Now neurogenetics is on the cusp of a landmark breakthrough. "Every now and then something happens that throws a field wide open and I think there's a feeling that we haven't had that breakthrough yet in neuroscience," he says.

"The great theory of how genes control the formation, structure and function of complicated nervous systems – we still don't have that in the bag yet, and my feeling is that neurogenetics can contribute hugely to our understanding of the brain."

One approach to neurogenetics is to trawl through genetic sequence information from vast numbers of people and seek common variants. It's a route that researchers have taken to look at DNA differences between individuals who have a mental illness and those who don't.

TCD has recently been involved in a number of such projects, where researchers from a number of international centres collaborate, explains Michael Gill, professor of psychiatry, based at St James's Hospital in Dublin.

"We have had three main programmes, one in psychosis, one in ADHD and one in autism," he says. "The three programmes require a very intensive clinical perspective with lots of cases and lots of good diagnostics, and we collaborate closely with the Trinity College Institute of Neuroscience and the psychologists, because part of the assessment is of what the symptoms and characteristics are and how it affects thinking and behaviour."

The genetic component of mental illness is often complex and seldom follows a simple pattern of inheritance, hence the need for large cohorts of patients to analyse what's going on, says Gill, who says collaboration is key. "No one site has enough samples to tease these things out by themselves, unless you are fortunate enough to come across unusual situations or families," he says. "So if it's 4pm, we have a teleconference with collaborators in the US."

Pooling resources pays off, with recent results uncovering new aspects of genetic differences between people with conditions such as schizophrenia and bipolar disorder, and those without.

One study of over 3,000 patients with schizophrenia found they had a slightly increased rate of "copy number variation", where stretches of DNA are replicated or missing, and in a small number of patients the researchers identified deletions on areas of chromosomes 1, 15 and 22.

Another study of over 4,000 people with bipolar disorder has also thrown up some tantalising clues, with variations cropping up in genes involved in the function of ion channels that help control brain cell activity.

"It took the combination of the very big patient cohorts and the developing technology to be able to really look at differences between patients and controls and get a handle on what's going on. And that's only really still under way," says Prof Gill.

Increasing our understanding of the genetics behind mental illness could lead to improved interventions like treatments or reducing the risk of developing a condition, he adds. "When I see the effect that schizophrenia or autism has on a person, the thought of being able to prevent those conditions would be a big thing."

And it's not just human brains that interest researchers at TCD.

Flies can also help shed light on how brain cells wire together and function. It's about looking at how genes work, according to Prof Mani Ramaswami, who studies how neurons change during learning and the formation of memory.

"It is important to appreciate what 'how' really means in the context of the nervous system," he says, describing how his research looks at the sites where gene products are active in the brain, how experience controls their activities, and how their activities change the properties of brain cells and alter perception and behaviour.

Using the fruit fly (Drosophila) as a subject allows the researchers to tightly control and examine genes and brain cell function. "The fly is an organism par excellence for understanding mechanisms of perception and memory," says Ramaswami. "In addition, it has become an excellent model for studying heritable forms of human disease, for understanding the underlying biology and for identifying lead compounds to modify for drug development."

Other neurogenetic research at TCD includes looking at how genes affect brain cell identity and wiring, with Dr Kevin Mitchell and Dr Juan Pablo Labrador researching animal models, while work continues on the genetics of blindness, as the eye is part of the brain.

"We feel that there's something remarkable to come and it's great that we have a group of neurogeneticists doing a lot of good work in Dublin and in our own department," McConnell says.

"It's not to say there are not other great challenges, there certainly are, but for me it's the great puzzle – how does the brain work? And ultimately we are interested in the relationship between the brain and memory, emotions, mathematical ability, the ability to paint. And I think genetics is helping and can help to find the 'DNA moment' – the turning point," says McConnell.

TCDGeneticsat50

A SPECIAL REPORT

Relying on genetics for future food supply

Worldwide food shortages mean that the production of genetically modified crops may not always be an option, but instead an essential practice, writes **Ronan McGreevy**

Worldwide food shortages are resulting in high prices for staple foods, such as rice, in many developing countries. Photograph: Reuters

THE RECENT rise in food prices serves as a warning to people about the potentially devastating effects of food shortages. Though the spike in the prices of commodities such as bread and milk caused pain to those on low incomes in the developed world, it also went on to prompt riots in Haiti, Cambodia, Indonesia and India as basic foodstuffs, such as rice, were priced out of the range of ordinary people.

The worldwide food inflation was caused by a number of factors, such as the conversion of millions of hectares of lands from cereal crops to bioethanol, and droughts in Australia and India. Another key factor is growing prosperity in the world's two most populous countries – India and China – leading to a spike in the consumption of meat which demands much more intensive farming.

The pressure on food supplies is likely to get worse. According to the UN, the world's population will increase from 6.7 billion today to 9.3 billion by 2050.

"That's the equivalent of the population of Germany being added every year," says Tony Kavanagh, Associate Professor of Genetics in Trinity College Dublin (TCD).

Kavanagh is passionately progenetically modified (GM) foods which have had a bad public profile since the first transgenic plant – a tobacco plant resistant to an antibiotic – was created in 1983.

They have been called "Frankenstein foods", and Minister of State for Food and Horticulture, Trevor Sargent, wants Ireland to be a GM-free nation, recently calling GM foods a "dangerous distraction from the fundamental challenges" of future food supply.

Unlike other parts of the world, the EU has been circumspect about introducing GM foods and the area under cultivation is much smaller than in the rest of the world.

At TCD they take a different view. GM foods, they say, are not an option – they are essential if the world's burgeoning population is to be fed at a time when global warming is showing signs of wreaking havoc on agriculture.

"To solve the problems of future food supplies, we're going to have to throw everything at it. We have a really useful tool which is GM technology. Not to use it would be crazy," says Kavanagh.

He believes that without the "green revolution" of the 1960s, which saw the cultivation of high-yielding varieties of wheat and rice, countries such as India would still be experiencing periodic famines. In India, for example, a new rice variety capable of yielding up to 10 times more than local varieties, revolutionised agriculture and food security. The country has not experienced famine since green revolution agriculture was introduced in the late 1960s.

"From a scientific point of view, we have had 25 years of GM crops. None of the scare stuff has held up and yet [GM opponents] are still banging on about it," he says.

Currently, GM crops account for 57 per cent of soybean, 25 per cent of maize, 13 per cent of cotton and 5 per cent of oil seed rape worldwide. In the US alone, 90 per cent of soybean, 85 per cent of cotton and half of all maize are GM crops.

"One of the real problems about the criticisms in the West is that those who pontificate from their affluent position do not know how critical this is because they don't have to," Kavanagh says.

One of the biggest proponents of GM crops is the giant multinational corporation Monsanto. Its biotechnology manager Dr Chris Merritt says food surpluses in Europe may become a thing of the past.

Pressure on food stocks elsewhere could restrict the flow of imports, such as foodstuffs for animals, which have to be imported from outside Europe, he believes.

"We were in a luxury situation where we were producing surpluses and food prices were low. Opposition to GM did not matter. Now that things have changed, people are beginning to ask if we should use the most efficient agriculture again.

"In the UK we have blight-resistant potatoes which were harvested recently. That's an example of a crop which could really benefit us, particularly in wet years like we have now, where blight is a big problem and crops have to be sprayed nine or 10 times."

David McConnell, Professor of Genetics at TCD, says the opposition by the Green Party and others to GM foods is not only wrong, it is potentially damaging to Ireland's standing in the scientific community.

"It is misleading everybody in the country, including students of science. It will cause significant disadvantages to consumers, farmers and food producers.

"There is no doubt that some anti-GM people have set out to cause fear and anxiety. They are the modern-day equivalent of flat-earthers," he says.

Currently, TCD scientists are investigating fundamental genetic questions about how plants grow, by using GM crops as a research tool. "We're interested in, for instance, if plants can be used as a production platform to produce antibodies and to produce other kinds of therapeutic new proteins," says Kavanagh.

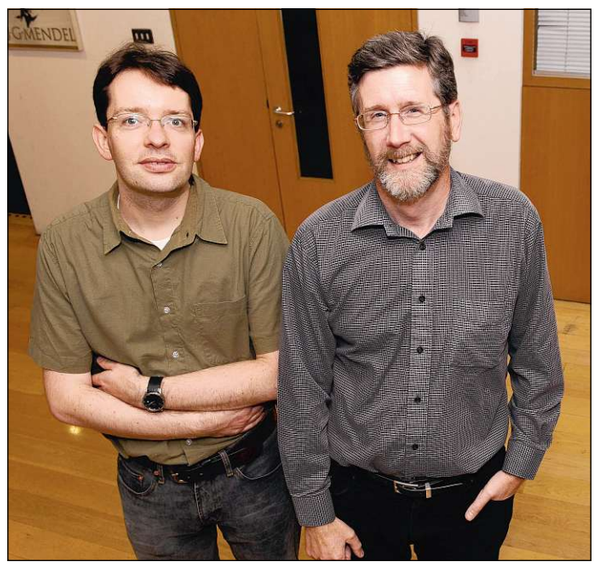
Dr Frank Wellmer, another faculty member involved in plant research, is studying GM versions of mouse-ear cress, a weed that can be found in any garden.

"The research is focusing on the development of flowers which carry the reproductive organs of a plant, ultimately giving the seeds that lead to reproduction.

"When you learn more about how flowers form, you may have a good starting point so that you can manipulate plants so that they give higher yields," he says.

Though the mouse-ear cress has no agricultural properties it is very similar genetically to important plants such as oil seed rape, cauliflower and mustard.

The research carried out at TCD aims at understanding the molecular processes that control the growth and development of higher plants. Any progress that will be made in understanding their development has potential applications in plant breeding.



LEADING THE GM REVOLUTION
Dr Frank Wellmer (left) and Prof Tony Kavanagh from TCD's Department of Genetics. Photograph: Aidan Crawley

■ **Dr Frank Wellmer** is a German scientist who obtained his PhD at the University of Freiburg in 1998. He carried out post-doctoral research between 1999 and 2005 at the California Institute of Technology and became a senior research fellow between 2005 and 2006. He has lectured at the Smurfit Institute of Genetics since September 2006.

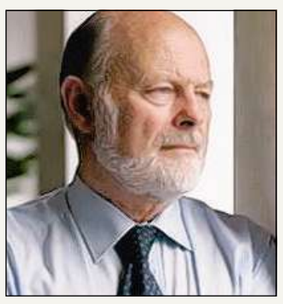
■ **Prof Tony Kavanagh** is Associate Professor of Genetics at Trinity College Dublin. He obtained his doctorate from UCD in 1984 and, following post-doctoral research at the Plant Breeding Institute in Cambridge, returned to his current position as head of the Plant Molecular Genetics Laboratory in Trinity in 1987.

Profile Prof Patrick Cunningham, chief science adviser

IN THE early days of genetics at Trinity, Prof George Dawson formed an alliance with TCD's Department of Agriculture – Profs Paddy Cunningham and Vincent Connolly of that department delivered classes in animal and plant genetics. Cunningham is now chief science adviser to the Government.

Cunningham graduated from UCD in 1956 in agricultural science. He completed an MA in animal nutrition, then went to Cornell University for a PhD in animal genetics.

In the 1960s, he took a research position with An Foras Talúntais (now Teagasc).



Appointed head of department in 1970, 10 years later he accepted the position of deputy director of research.

In 1964 Cunningham joined TCD's Department of Genetics and was appointed professor of animal genetics in 1974.

In 1990, he took up the post of director of animal production and health at the Food and Agricultural Organisation (FAO) of the UN.

Cunningham returned to TCD in 1989 to establish a new programme of research into the improvement livestock health.

In 1996, Cunningham and his team developed a system of DNA traceability. They then established IdentiGEN, which deploys these technologies in Europe and in the US.

Experts to explain genetics to the public

PETER McGUIRE

GENETICS HOLDS the key to understanding our natures. DNA in criminal trials, genetically modified food, the origins of HIV/Aids and genetic health will all feature among issues discussed by international experts at a public symposium to mark 50 years of genetics at Trinity College Dublin (TCD).

The symposium takes place this Saturday, from 11am-6pm, at D4 Hotels Ballsbridge Inn (formerly Jury's), Pembroke Road, Dublin 4.

Prof Steve Jones, a top evolutionary geneticist from University College London, will discuss the topic *Is human evolution over? - the view from the genes* (beginning at 11.30am). Humans and chimpanzees evolved from a common ancestor, and we share the vast majority of our genetic material with them. Natural selection, it would appear, is still at work.

Paul Sharp, professor of genetics at the University of Edinburgh, will further highlight our evolutionary and genetic merry-go-round with a talk on *Tracing the Origins of HIV* (at 2.40pm). How are some people genetically resistant to HIV, a disease that first evolved among primates?

***Feeding the world: Genetics in the lead*, a talk by Prof Patrick Cunningham of TCD (at 3.40pm), will focus on the challenges presented to the world's food supply by a growing population.**

***Genetics gets personal: how to read your genome, and what it means for your health*, will be presented by Dr Brian Naughton (at 12.10pm), founding research and development architect at 23andMe (23andme.com), a personal genetics company.**

Rockne Harmon of the San Francisco District Attorney's Office – prosecutor at OJ Simpson's trial – will explore (at 2pm) *Forensic DNA typing: are we realising its full potential?*

Finally, Dr Stephen Minger of King's College London will talk about *Stem cells: a new frontier*, explaining the science behind this treatment (at 4.20pm).

The audience will be free to ask questions, and the day will finish with a general discussion at 5pm.

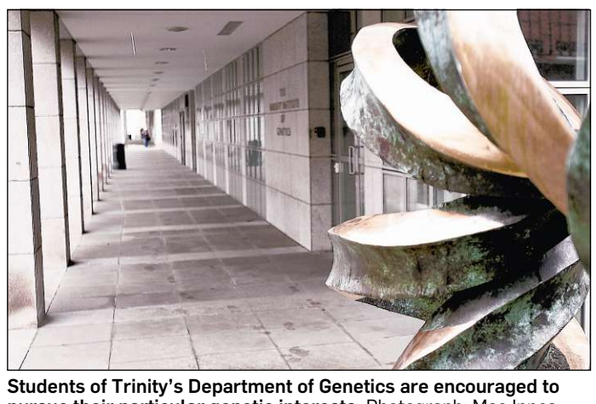
"Some people may attend because these issues can be controversial," says David McConnell, Professor of Genetics at TCD. "I hope they will attend because they are interested, and will leave feeling that experts have helped them to understand the science behind these issues."

■ Tickets at the door (€5). For more information see genetics50.org

■ All former members and graduates of the department are invited to join a symposium today and tomorrow, with lectures held in the Joly Theatre at the Smurfit Institute of Genetics in Trinity College. Talks on evolutionary genetics, neurogenetics, plant genetics and more will be given. See genetics50.org/programme.php

Becoming a student at Trinity

There is more than one way to study genetics in Trinity College, and more choices open up once you have taken that first step, writes **Louise Holden**



Students of Trinity's Department of Genetics are encouraged to pursue their particular genetic interests. Photograph: Mac Innes

ARE YOU interested in the evolution of man? Or maybe you prefer yeast and pox viruses? Perhaps you want to know how we can use genetics to discover new antibiotics or increase food production? Or if you'd like to delve into the story of life, genetics is a good place to start.

Trinity College Dublin (TCD) is now among the best-known centres of genetic teaching and research in the world. High-level genetics teaching and research is going on in the college – and not just in the Smurfit Institute of Genetics, but in other departments, such as zoology, psychiatry, medicine, chemistry, biochemistry and, especially, microbiology.

Genetics is a discipline in the same sense as physics – to master it, you need to specialise. There are two ways to specialise in genetics at TCD.

If you take the undergraduate science programme – TR071 – you will have the option of moving into genetics in your third year. From that point on, you are encouraged to follow your own particular genetic interests.

The other, more direct approach, is to take on the TR073 degree programme in human genetics. "This is a more tightly-prescribed course," says Prof David McConnell of the Smurfit Institute of Genetics.

"It's competitive and only 15 places are offered each year. As a result, the points requirements tend to be quite high – but well within reach of students who have a strong interest in science or medicine. An education in genetics is a wonderful general preparation for life," McConnell says.

"It's a challenging area that places emphasis less on memory and more on logic and imagination. Biology and chemistry are useful bases. However, it's not unusual for students with an interest in physics or mathematics to find their way into genetics."

Much genetic research is concerned with the structure of genes at the molecular level and how they affect organisms.

"Take the protein rhodopsin," says McConnell. "It sits in the cells of the retina, and it is coded for by a gene. So, how does a gene decide to make rhodopsin in the retina, and nowhere else? These are the sorts of puzzles that genetic researchers are working on, especially on how mutations in the rhodopsin and other genes cause blindness."

This is just one example of the work going on in the university, which is highly-respected worldwide for covering the main lines of thinking in genetic research.

A genetics student at TCD has a broad portfolio of subjects to choose from, as there is high-level research activity underway across the spectrum. Some fields are not as well-known as others.

"Quantitative genetics, for example, is the study of the affect of genes on measurable characteristics such as wheat yield or milk yield," says McConnell. "This field of research is very important because it allows us to examine the interplay between genes and environment."

Population genetics is another important discipline, says McConnell. "By looking at the frequency of genetic variants in populations, we can find out the origin of those populations," McConnell explains. "There is evidence that we are closely related to the Basques."

Other research is being carried out in the field of neurogenetics, the study of how our genes shape the growth and function of the nervous system.

According to McConnell, this links into other studies in neuropsychiatric genetics. "As we learn more about the genetics of the nervous system we will gain more insights into how the brain works – the genetic basis of memory and language, or musical or mathematical talent, for example," says McConnell.

Plant genetics is another important area of activity in TCD. "Norman Borlaug, a geneticist, won a Nobel Prize for peace for his work on plant genetics – that tells you the importance of this field," says McConnell. "His work contributed to a massive increase in food production and staved off famine in Asia and Latin America.

"We also have a very strong interest in evolutionary genetics which relates to research on antibiotic production and resistance – critical to health," he says.

Prof Seamus Martin is one of the top experts in the world on the genetics of apoptosis, or why cells die – a critical question in cancer research.

In an allied field, Dr Adrian Bracken, who collaborates with doctors at Tallaght Hospital, is examining the control of genes in cancer cells.

"We offer our students a broad but rigorous curriculum in genetics," says McConnell. "There are more research students in the Smurfit Institute than undergraduates. In the final year there are about 25 undergraduates and 15 members of staff. All students carry out a research project."

The Vincent Scholarships support six third-year students to spend between two and three months in US laboratories as summer interns. "Our undergraduate programme is strong and challenging, but students rise to the challenge," says McConnell.

"A striking feature of the department is the high number of genetics researchers that we produce," he says. "Two-thirds of all of our graduates go on to become research scientists and many are working in the field at high levels all over the world. However, we say that geneticists can do anything – our graduates have become lawyers, doctors, patent attorneys and teachers."

■ For more information, see tcd.ie/Genetics/ and tcd.ie/Microbiology/