





Advances and Challenges in the Systemic Treatment of Cancer - towards a personalised approach

Prof Maeve Lowery, Prof of Translational Cancer Medicine, TCD Academic Director, TSJCI

Cancer described since earliest records...



- Earliest description of cancer approx. 3000 BC
- "There is no treatment"



Term 'Cancer' dates from 300 BC...

- Origin of word cancer from Hippocrates
- 1st proponent of 'personalised therapy'



 "different [drugs] to different patients, for the sweet ones do not benefit everyone, nor do the astringent ones, nor are all the patients able to drink the same things."

What is cancer?

- Cancer = a malignant growth
- Growth of cells is uncontrolled
- Cells can spread to nearby & distant sites
- <u>Grade</u> How bad do the cells look?
- <u>Stage</u> Where has the cancer spread?



Indication for systemic therapy:

- Primary site of tumour
- Grade How bad do the cells look?
- Stage Where has the cancer spread?
 - <u>T</u>umor
 - <u>N</u>odes (Lymph)
 - <u>M</u>etastases
- Biomarker assessment (IHC, NGS, blood based ...)







Cancer Treatment: Chemotherapy



- Chemotherapy stops cancer cells from growing, dividing & making more cells.
- Cancer cells grow & divide faster than normal cells, so chemotherapy has more of an effect on them.
- But it still has side effects...

Chemotherapy side effects....



How can we do better?



Immunotherapy



Targeted Therapy

Precision Medicine



- All humans are all different.
- What is best for one individual may not be best for another.
- How can cancer care respect these differences and leverage them to optimise treatment?

Precision Cancer Medicine "a new era"



Cancer Generating Pathways



Causes of Cancer





Nature education 2010

Cancer.gov

Cancer Genetics: "Targeted Therapy"



Cancer Genetics: "Targeted Therapy"



- Genes can be turned on and off in cancer cells
- Studying this allow us to develop drugs that block the growth and spread of cancer by interfering with specific molecules ("targets") involved in cancer growth

Mutations are Therapeutic Targets





Lynch et al., NEJM, 2004

<u>Melanoma</u>







Flaherty et al., NEJM, 2010

Targeted therapy : Melanoma



Flaherty et al., NEJM, 2010

Immuno-oncology



Cancer Therapy: Immuno-oncology



 New Immunotherapy drugs help the patients immune cells to recognise cancer cells as foreign and begin to attack...

Tumour microenviroment as a target : Immune checkpoint blockade



Biomed Res Int. 2015, Larkin NEJM 2015

CAR T Cell Therapy



Lekha Mikkilineni, and James N. Kochenderfer Blood 2017;130:2594-2602

Tumour Infiltrating Lymphocyte Therapy



- Surgically remove a piece of tumor
- Dissect the tumor to isolate TILs
- Expand in lab
- Infuse back to patient
- TILs actively destroy cancer cells & leave healthy cells unharmed

Not all cancers respond to immunotherapy...



- Some cancers block the immune cells from reaching the tumour "cold"
- Some cancers are full of immune cells which activate quickly in response to immunotherapy drugs "hot"

Translational research to personalize care...



Organoids

- 3D multicellular in vitro tissue construct that mimics its corresponding in vivo organ
- Characteristics
 - 3D interactions between cells mimic patient physiology
 - Long-term culture possible
 - Suitable for (high-throughput) drug screening
 - Sensitivity to treatment reflects patient response



PancREatic Cancer OrganoiDs rEsearch - PRECODE

- Marie-Curie ITN
- Objective: establish a European resource of organoids from PaCa and to identify new target for disease treatment.
- Project TCD: Genomic analysis and functional profiling of DNA repair for identification of targetable DNA damage repair defects



HEALED CONSORTIUM

HEALED

🤣 RemedyBio 🔶

Patented mass scale single cell nanoreactor technology to isolate TILs







Investigate the role of tumour microenvironment (TME) and inflammation in regulating the effectiveness of TIL therapy



Sequence data generated by SJH/TCD to develop a novel deep learning algorithm for neoantigen prediction.









Expand cells with GMP modular hub co-located with St. James's Clinical Research Facility

lector

Young onset cancers – an increasing problem...



Martin C S Wong ¹ ² ³, Junjie Huang ¹, Paul S F Chan ¹, Peter Choi ¹, Xiang Qian Lao ¹, Shannon Melissa Chan ⁴, Anthony Teoh ⁴, Peter Liang ⁵









Fear of Cancer Recurrence in Cancer Survivorship



Catherine O'Brien, PhD Candidate Advanced Nurse Practitioner Cancer Survivorship,

Trinity St James's Cancer Institute Survivorship Group

Precision / Personalised Medicine



- All humans are all different.
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Personalising cancer care for people with intellectual disabilities...

- Make communication simple and clear pictures and easy-read materials.
- Include caregivers and allow extra time for appointments.
- Train staff to understand the specific needs of people with intellectual disabilities
- Develop specialized centres with dedicated support e.g
 - Intellectual disability specialist oncology nurses
 - Community liaison
 - Social work



Trinity St James's Cancer Institute

Thank you