



Pillar 1; A systematic approach to radiobiology

Dr. Emma Melia
21.05.26



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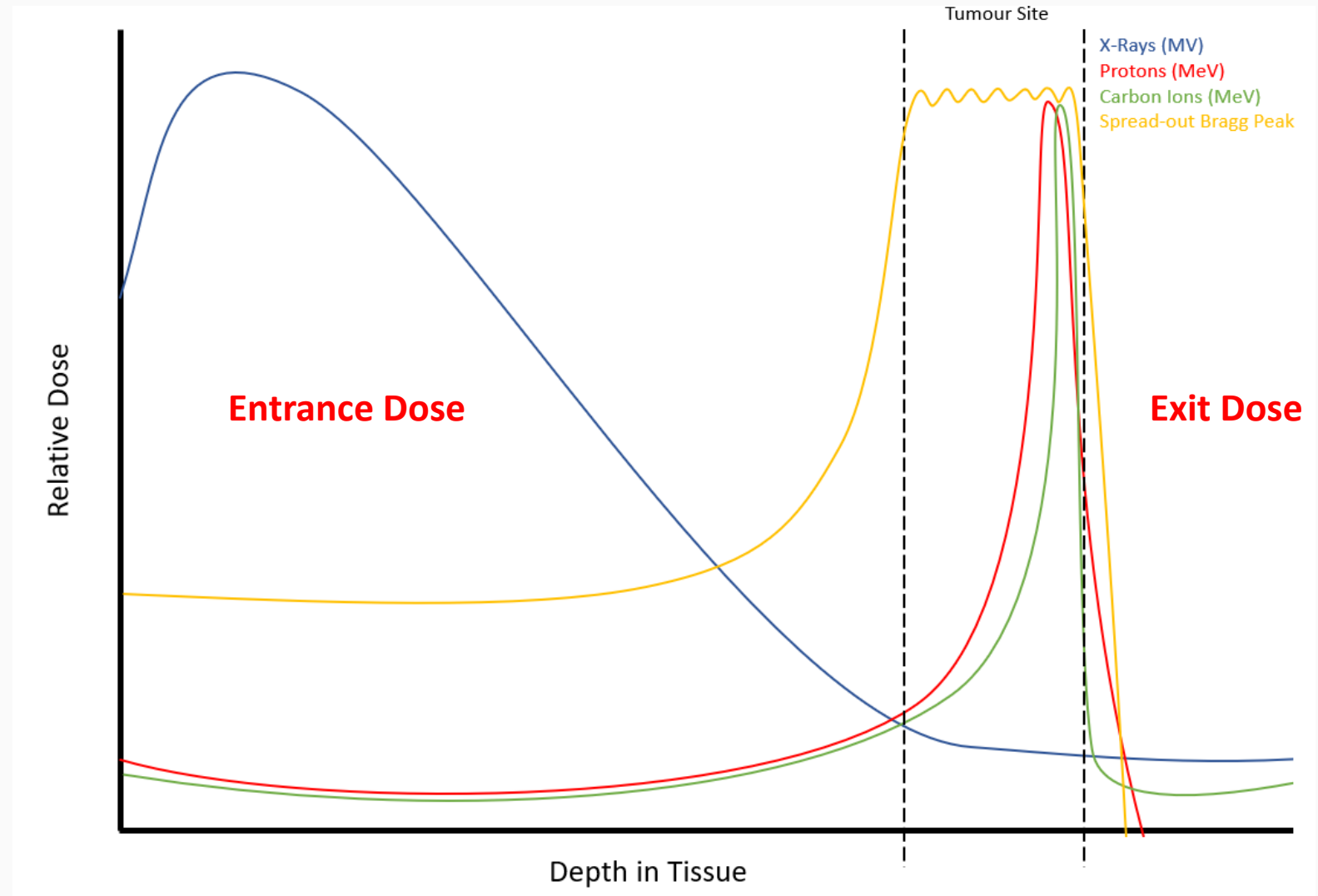
CANCER
RESEARCH
UK

RadNet
Birmingham



Particle Therapy

- Different particle types
- SOBP – Spectral energies
- Variation in modality characteristics – energy, LET



Current facilities for investigating radiobiology

- Conventional sources – linac/cyclotron/synchrotron

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Fabbrizi, et al. (2025)

- Laser-driven sources



QUEEN'S
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BELFAST



Lawrence Berkeley
National Laboratory

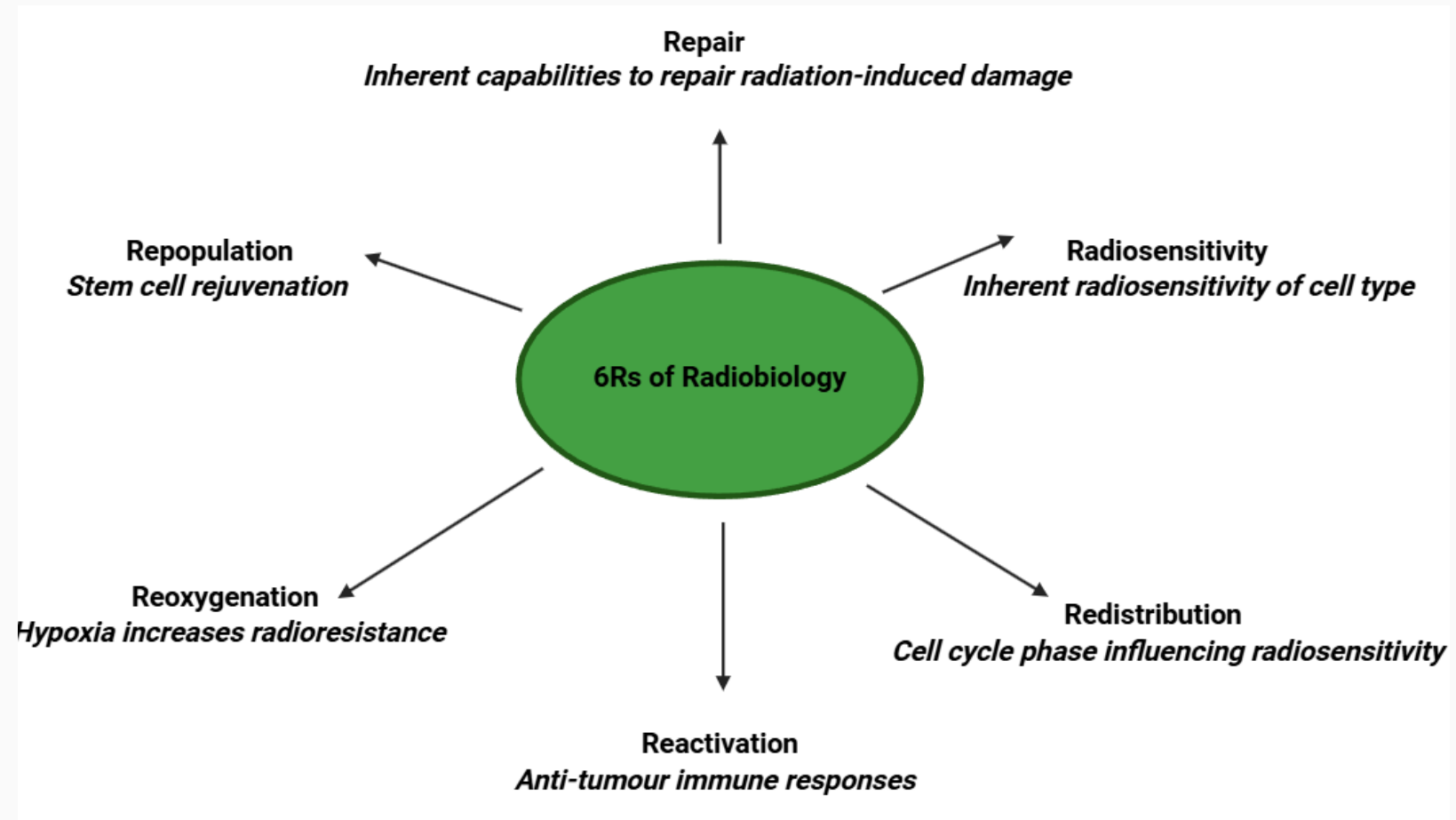
- Struggles for full radiobiology end points:
 - Irradiation spot sizes
 - Uniformity in dose
 - Proton energy variation
 - Shot-to-shot variation
 - Available ion species



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Radiobiology

- DNA damage and repair
- Tumour microenvironment
- Immune responses

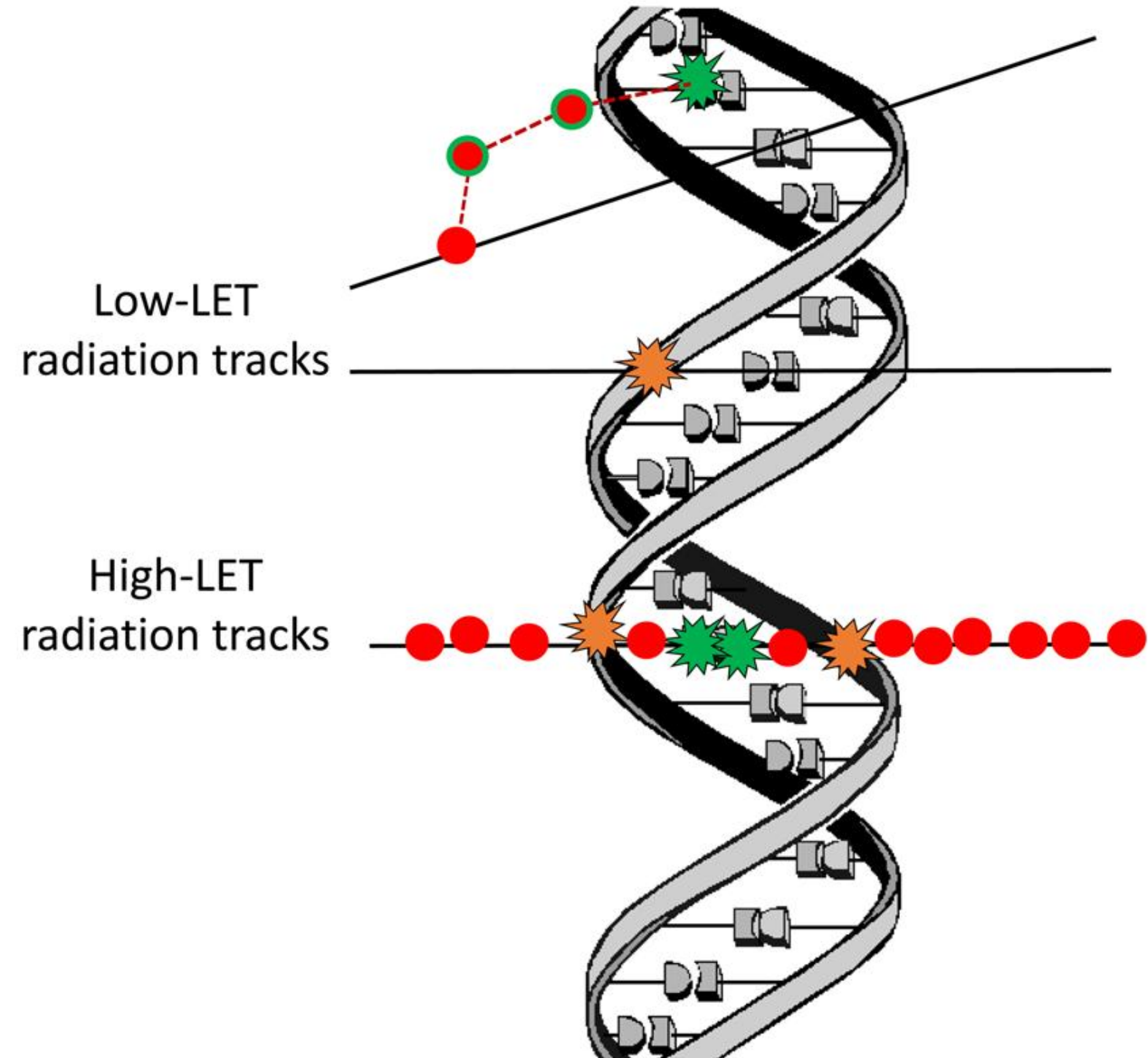


DNA Damage and Repair

- Type of damage depends on the radiation modality and LET;
 - Base damage
 - Single-strand breaks
 - Double-strand breaks
 - Complex/clustered DNA damage
- Various repair mechanisms determined by;
 - Cell cycle stage
 - Mutational profile
 - Protein expression or activation
 - Hypoxia (low oxygen concentrations)



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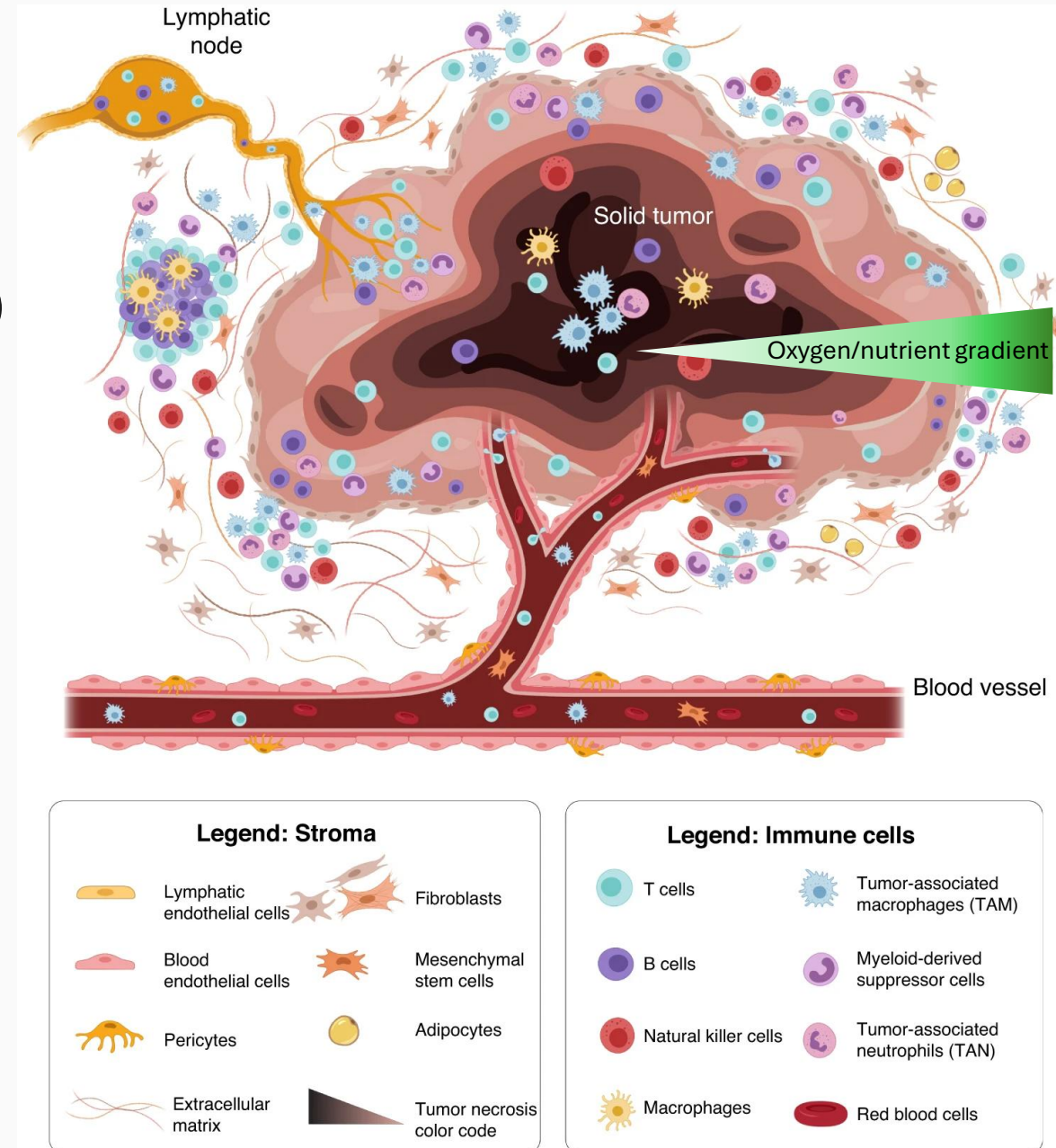


Tumour Microenvironment

- Vasculature
- Stromal cells (Cancer-associated fibroblasts)
- Extracellular matrix
- Signalling molecules
- Hypoxia (low oxygen concentrations)
- Immune infiltration

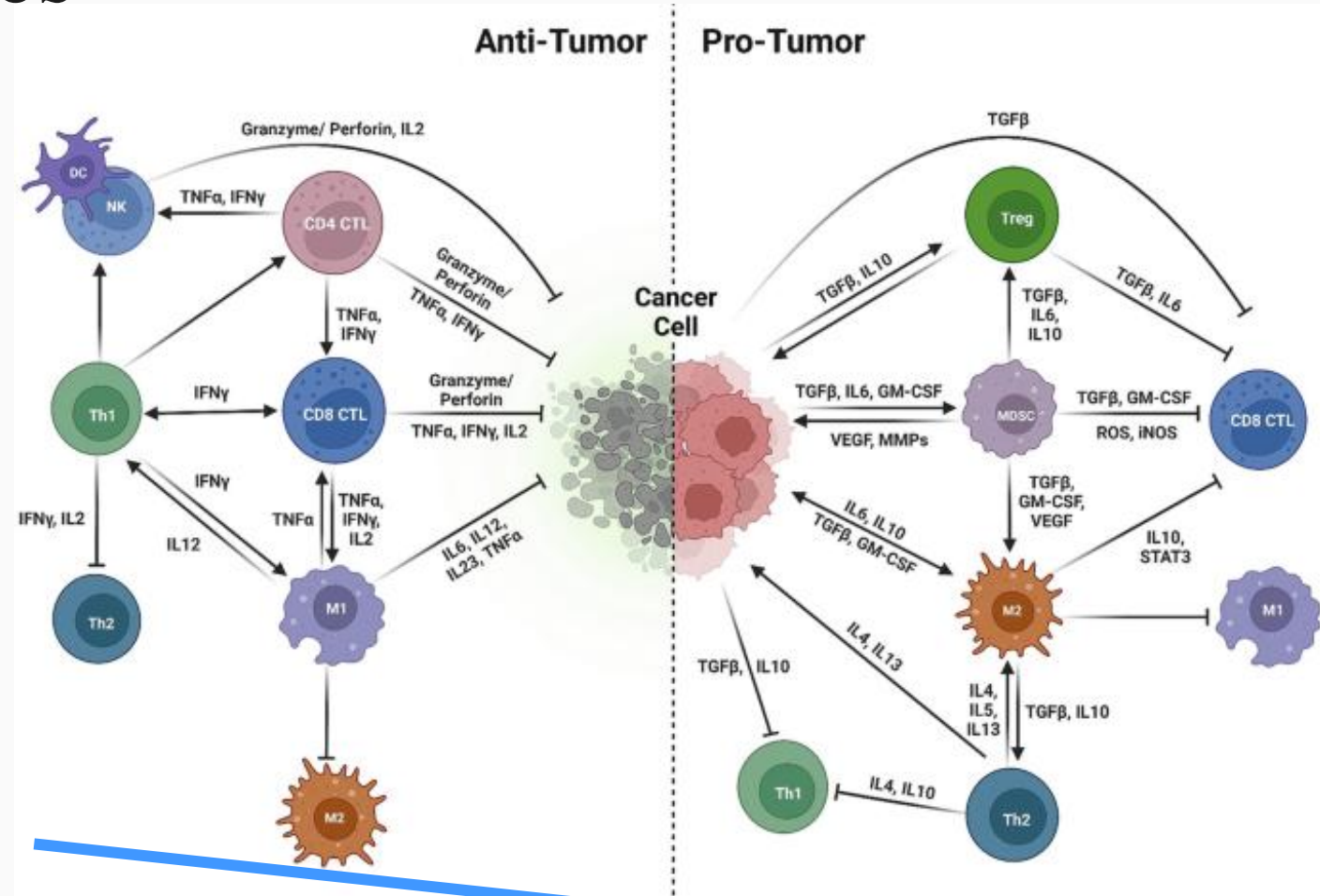


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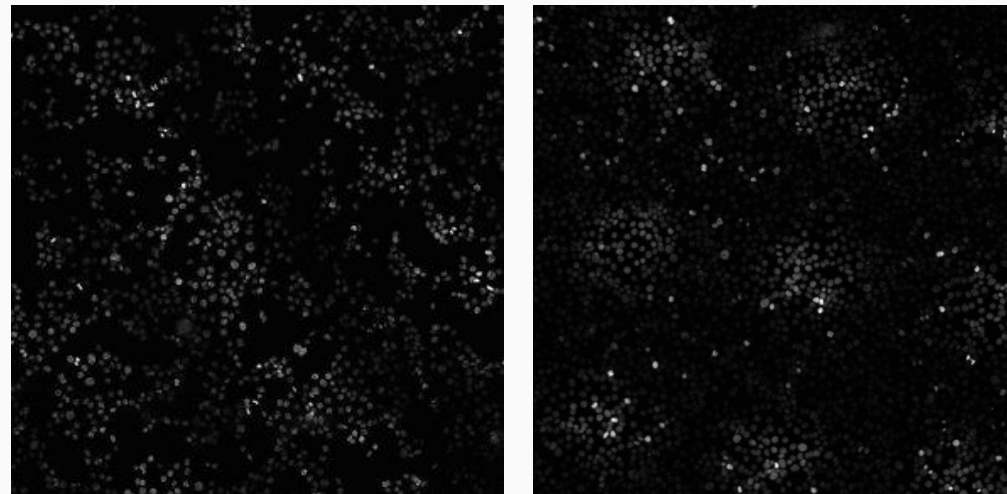
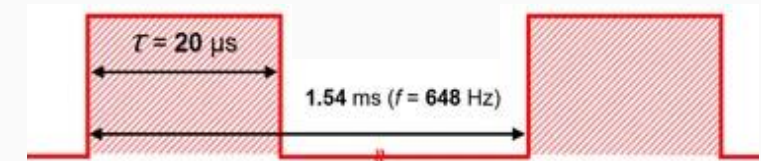
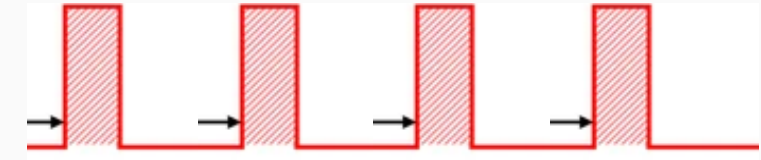
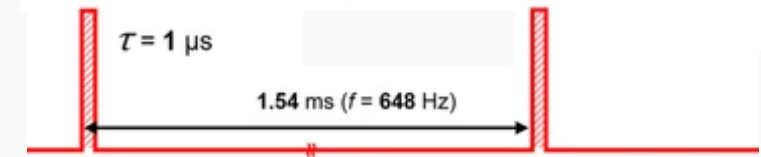
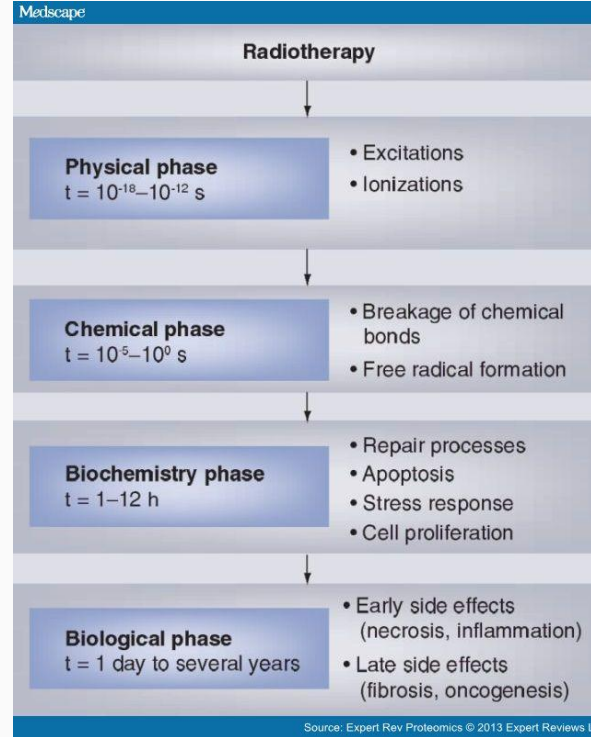
Immunological responses

- Immune infiltration – local or systemic response?
- Uncertainties:
 - Does the radiation modality matter?
 - Does LET influence immune activation?
 - How does dose-rate or spatially fractionated beams alter immune responses?
 - Can these approaches synergise with existing immunotherapies?



Beam factors that could alter tumour response

- Dose
- Dose-rate
- Pulse structure
- Spatial fractionation
- Particle type, energy and LET



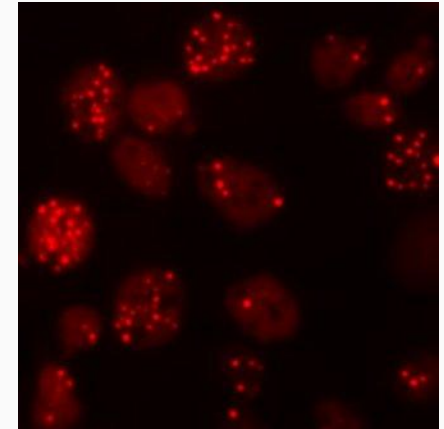
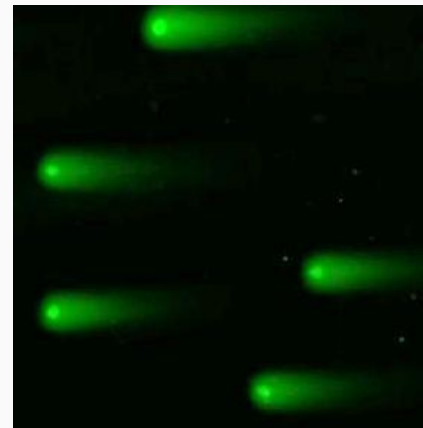
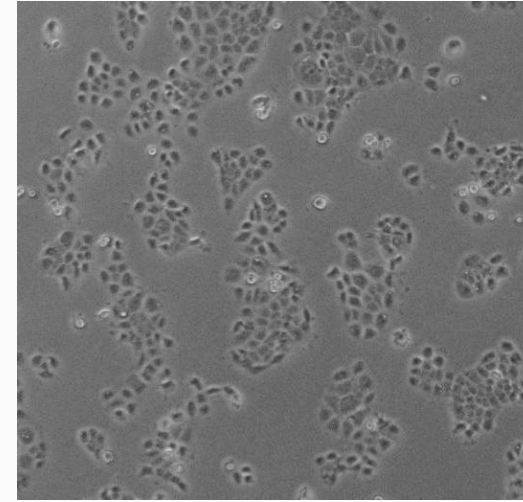
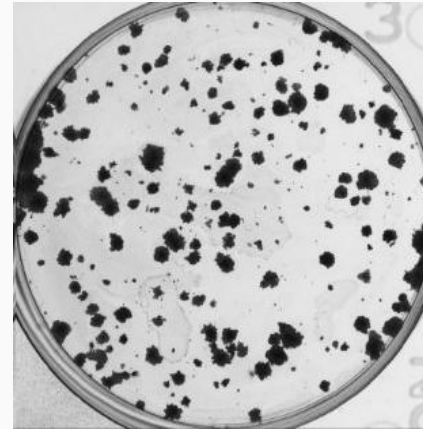
How do we get there? From cells to patients

- **2D** – fundamental responses, critical for first understandings and insight into tumour cell responses
- 3D – more complex, clinically relevant models
- In vivo;
 - Chick embryos
 - Zebra fish
 - Mice

Essential for translational studies and development of clinical trials

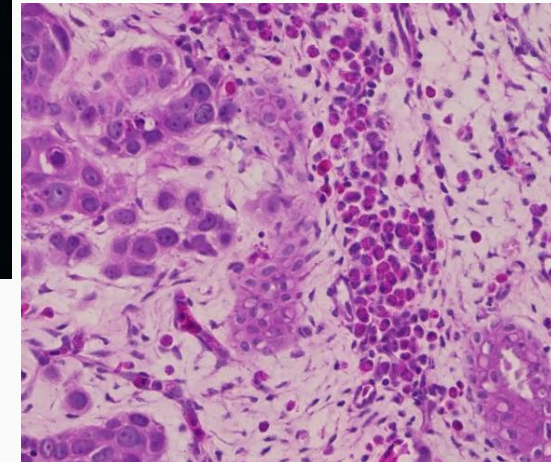
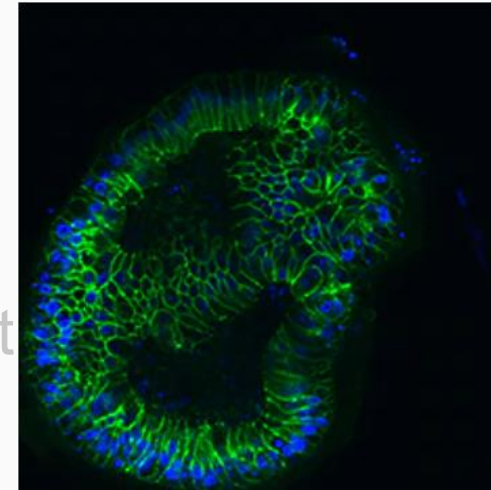
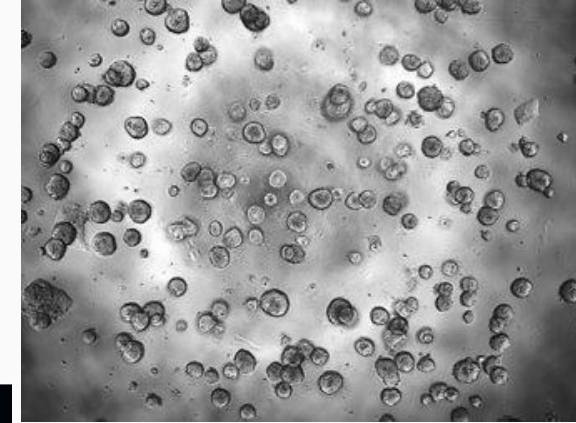
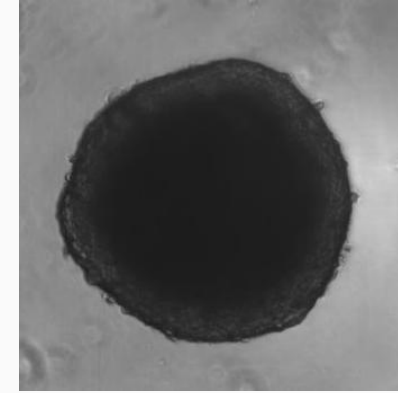


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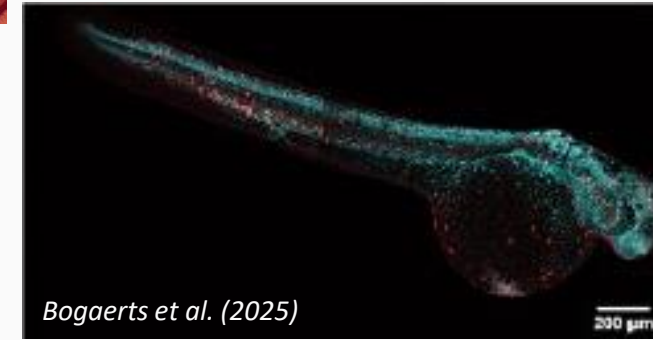
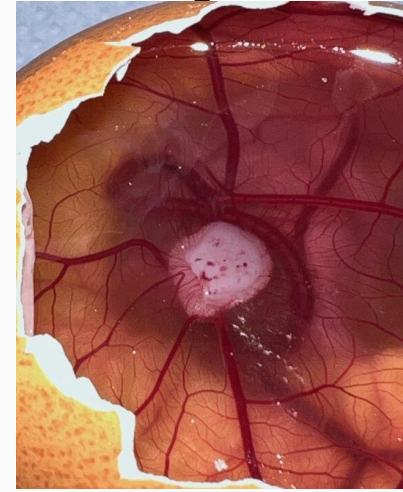
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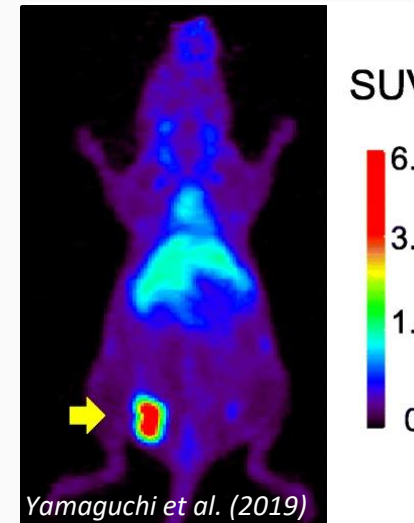
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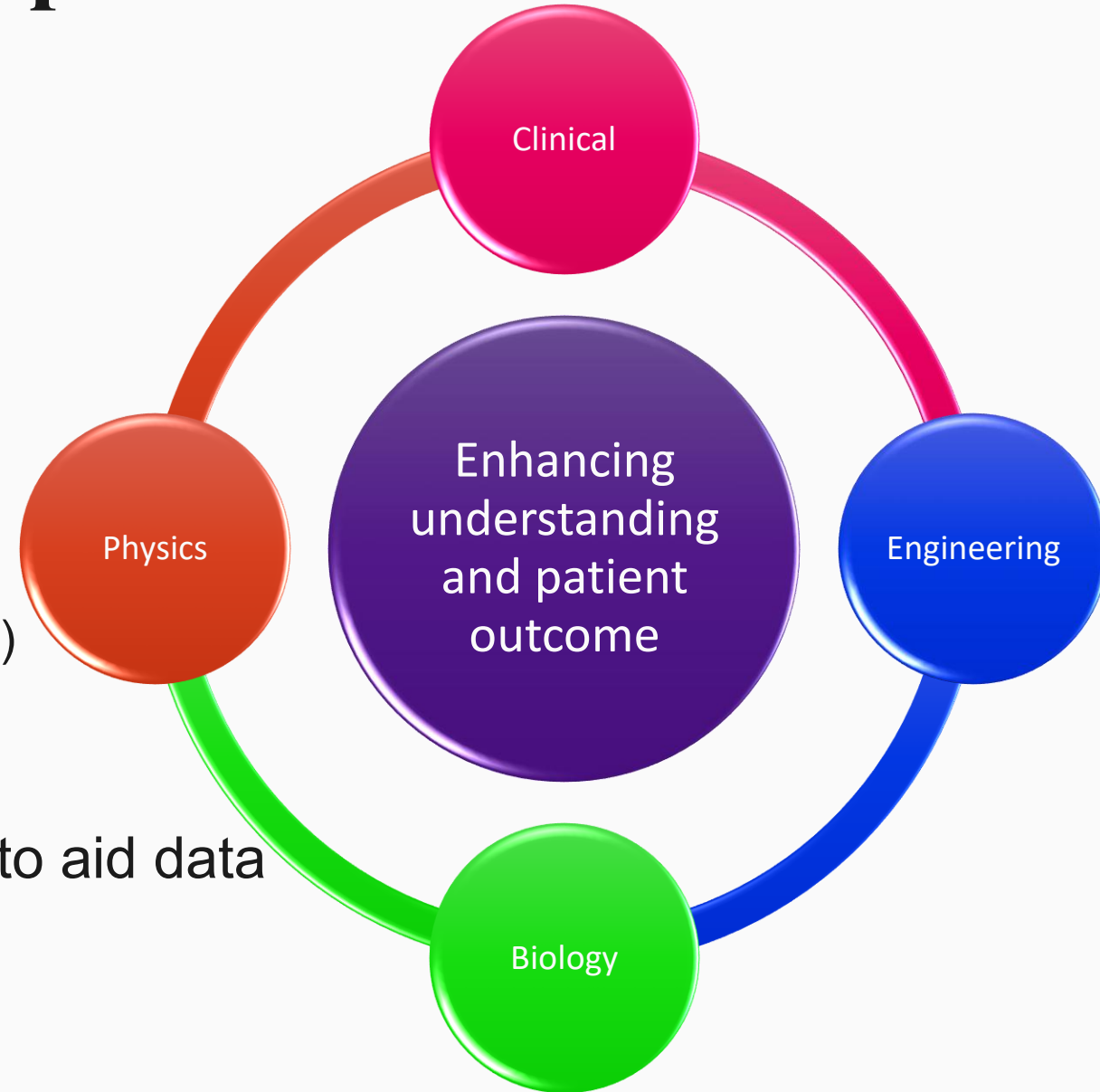
Bogaerts et al. (2025)



Yamaguchi et al. (2019)

Why is LhARA critical to help us achieve this...

- Flexible beam facility that can manipulate;
 - Ion species
 - Energy
 - In time and space
- Beam facility designed for radiobiology;
 - Beam characteristics and manipulation
 - High throughput biological end stations
 - Animal facilities
 - Radiobiology lab with state-of-the-art facilities
 - Customisable endstations (hypoxia, RT microscopy)
- Development of novel in beam diagnostics
- Generation of machine learning techniques to aid data interpretation



The LhARA Collaboration



Thank you!