Cancer ImmunoTherapy Accelerator (CITA)

Dr Shalini Jadeja
Develop novel immunotherapeutics, understand their mechanisms-of-action, and train a new cadre of scientists and clinicians able to develop, improve, interpret and deliver relevant immunotherapy trials.
The Vision

To develop an integrative London initiative that emerges as the UK hub for immunotherapy of cancer focusing on:

• Safe and effective new cancer immunotherapies from immune checkpoint blockade to adoptive cellular therapies
• Pre-clinical development of novel cancer-immunity-engaging therapies
• Training the next generation of basic and clinician scientists in cancer immunology
The Questions

1. What are the mechanisms underpinning response, resistance and toxicity to immunotherapeutic approaches?

2. Are poor responses or high adverse reactions to particular immunotherapeutics due to pre-existing differences in immune compartments?

3. Can we identify patients most likely to respond to therapy?

4. Can we anticipate, prevent and/or manage toxicities without compromising efficacy of the cancer immunotherapeutic in question?

5. Can we identify new immunotherapeutic targets in resistant cancers?
The CITA IMDC* Platform

**DNA**
- Next Gen sequencing
- Genetic alterations, ITH

**RNA**
- RNAseq/TCR Seq
- Transcriptional profiles
- NanoString

**Protein**
- Mass spectrometry
- Proteomic signatures
- Sciomics protein profiling

**Tumour and immune cells**
- Flow and mass cytometry
- Phenotypic characterisation
- Key regulatory components

**Tissue sections**
- Functional assays
- Topology of TME
- Immuno-histochemistry

---

Bioinformatic multi-level data integration with clinical response data

Identification of mechanisms and biomarkers of response, resistance, and toxicity

*Immune Monitoring and Discovery Core*
Charlie Swanton: Genomics, bioinformatics, GEnTILs
Sergio Quezada: GEnTILs, immunology, immunotherapy
Charlie Swanton: Genomics, bioinformatics, GEnTILs
Karl Peggs: ACT with GEnTILs and CARs
Javier Herrero: Bioinformatics
Hans Stauss: TCR-modified T cell therapies
Martin Pule: CAR-modified T cell therapies
Emma Morris: TCR-modified T cell therapies
Tony Ng: TME, Imaging
Kerry Chester: Immune-modulatory biotherapeutics
Teresa Marafioti: Multi-colour IHC, TME, IHC assay development
Ronjon Chakraverty: ACT, Adaptive immune-regulation /immune-activation

Adrian Hayday: Adaptive immune-regulation/ activation
Tony Ng: TME, Imaging

Charlie Swanton: Genomics, bioinformatics, GEnTILs
Julian Downward: Response and resistance, iGEMMs
Caetano Reis e Sousa: Adaptive immune-regulation/ activation, DCs and APCs
Gitta Stockinger: Adaptive immune-regulation/ activation, T cell subsets

James Larkin: Clinical trials
Martin Gore: Clinical trials

Kairbaan Hodivala-Dilke: Angiogenesis
Frances Balkwill: Inflammation
Biotherapeutic proteins and antibodies

• Expedite development of novel immune-modulatory biotherapeutics by generating high quality recombinant proteins.

• The Chester group have expertise in manufacture of recombinant proteins for both preclinical testing and clinical trials and use:
  – appropriate cell lines
  – defined materials
  – SOPs
  – product release criteria
Novel Immunogenic Genetically Engineered Mouse Models (iGEMMs)

- Generating novel iGEMMs by increasing immunogenicity in existing GEMMs by chemical and transgenic means (Walczak and Downward groups)
- Phenotype iGEMMs using IMDC platform and expertise of the 3i (infection, immunity, immunophenotyping) consortium [http://www.immunophenotype.org/](http://www.immunophenotype.org/)
- Make mice available to the Network and wider community
Immuno-Oncology Training

- Training on equipment and skills including:
  - IHC interpretation
  - Bioinformatics
  - Genomics & Proteomics
  - Flow Cytometry
  - Clinical Trials
  - Immune monitoring
- An annual Cancer Immunotherapies Symposium
- Networking Events and Career talks
Collaborative London-wide Network

• Encourage collaborations between Network members
• Share samples, outcome data (Toxicology & Efficacy parameters?)
• Allow comparisons and in depth analysis across trials e.g.
  – compare different PD-1 inhibitors in the same cancer
  – or the same inhibitor across multiple cancers
Pipeline for samples

Sample collection

Processing and storage according to CITA SOPs

Immune Analysis with CITA platform

Data Analysis

by CITA

by study/ trial team

by CITA ready for analysis

on site prior to transport for analysis
A. Simple: IMDC Platform-led
Analytical assays run as a service or with added technical expertise

Capacity: Dependent on available facilities, expertise and funds. Secondary sites for:

- Immune monitoring
- Biobanking
- Mass Cytometry
- Mouse phenotyping
- Biobanking
Collaborative working

2. Focus on interesting cohorts
Information collated from different centres on cohorts that are relapsing or behaving differently than expected

3. Novel approaches
e.g. vaccines, cell death

Complex: Requiring scientific scrutiny
Management scrutiny to decide which studies to support in part, if not fully

1. Routine analysis of samples from patients on approved Immunotherapy
   Analysing biopsies/ blood

Collaborative working
Criteria for studies to support

1. Samples collected and processed to our SOPs
2. Cohorts deeply phenotyped
3. Immunological analysis is a critical component
4. Academic sponsorship mandatory
5. Open/ near opening in the next 12 months
6. ‘Smart’ research questions (Novel, Innovative, Informative)
7. Why are you doing this and what will you learn?
8. Study/ Trial must have its own funding
9. Must be Powerful
10. Must include full analysis of data/ Quality Control

Please include the level and form of support required
The Paperwork aspect

• Ethics must permit sharing of data/samples

• Trial agreements must permit sharing of data/samples where possible

• Working with UCL legal teams to draw up suitable agreements to use for commercial companies
https://www.ucl.ac.uk/cancer/research/research-centres/immunotherapy-accelerator/enquiry_form

s.jadeja@ucl.ac.uk

Cancer Immunotherapy Study/ Trial Enquiry

* Required

Contact Details

Name of Trial/ Project *

Your answer

Contact Name

Your answer

Contact Email *

Your answer
Cancer ImmunoTherapy Accelerator (CITA)

Shalini Jadeja
s.jadeja@ucl.ac.uk
http://tinyurl.com/jpnx34t