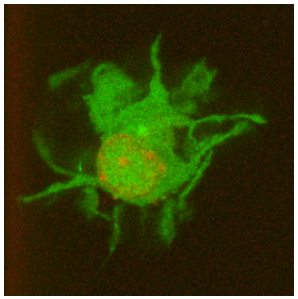
UNIVERSITY OF OXFORD

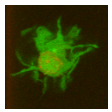


Oxford Immune Intelligence

Next Generation Dendritic Cell Platform for Breakthrough Therapeutic Outcomes

Executive Summary:
Next Generation Dendritic Cell Platform

- By initiating all immune responses and influencing their outcome, dendritic cells are attractive candidates for immunotherapy but first generation trials in oncology have shown limited efficacy
- OII's proprietary dendritic cell platform overcomes current roadblocks allowing production of either autologous or allogeneic 'off-the-shelf' cell therapy products
- The Company leverages world-leading science from Oxford University's Sir William Dunn School of Pathology and will exploit Oxford's comprehensive capabilities in translational medicine in collaboration with the Cell and Gene Therapy Catapult
- While the lead indication will focus on immuno-oncology, future applications will encompass tolerance induction to biological therapies in rare diseases, depending on investor appetite
- OII is seeking seed funding of £4.5m to establish pre-clinical PoC for its lead indication and readiness for first-in-man clinical trials



Founders

Paul Fairchild

Associate Professor of the Immunobiology of Stem Cells and founding Director of the Oxford Stem Cell Institute. Paul obtained his DPhil from the University of Oxford: the research he has since conducted at both Oxford and Cambridge Universities has led to first-in-man clinical trials for the treatment of non-small cell lung cancer, led by Asterias Biotherapeutics. He serves on the SAB of the UK Government's Cell and Gene Therapy Catapult

Marcelo Bravo

Serial entrepreneur with international experience in major blue chip companies as well as a number of start-ups bringing academic research-based innovation to market. Marcelo has taken two companies public to the AIM market, raising over £45m, mostly from institutional investors but also from family offices and HNWs.

Clinical Collaborators

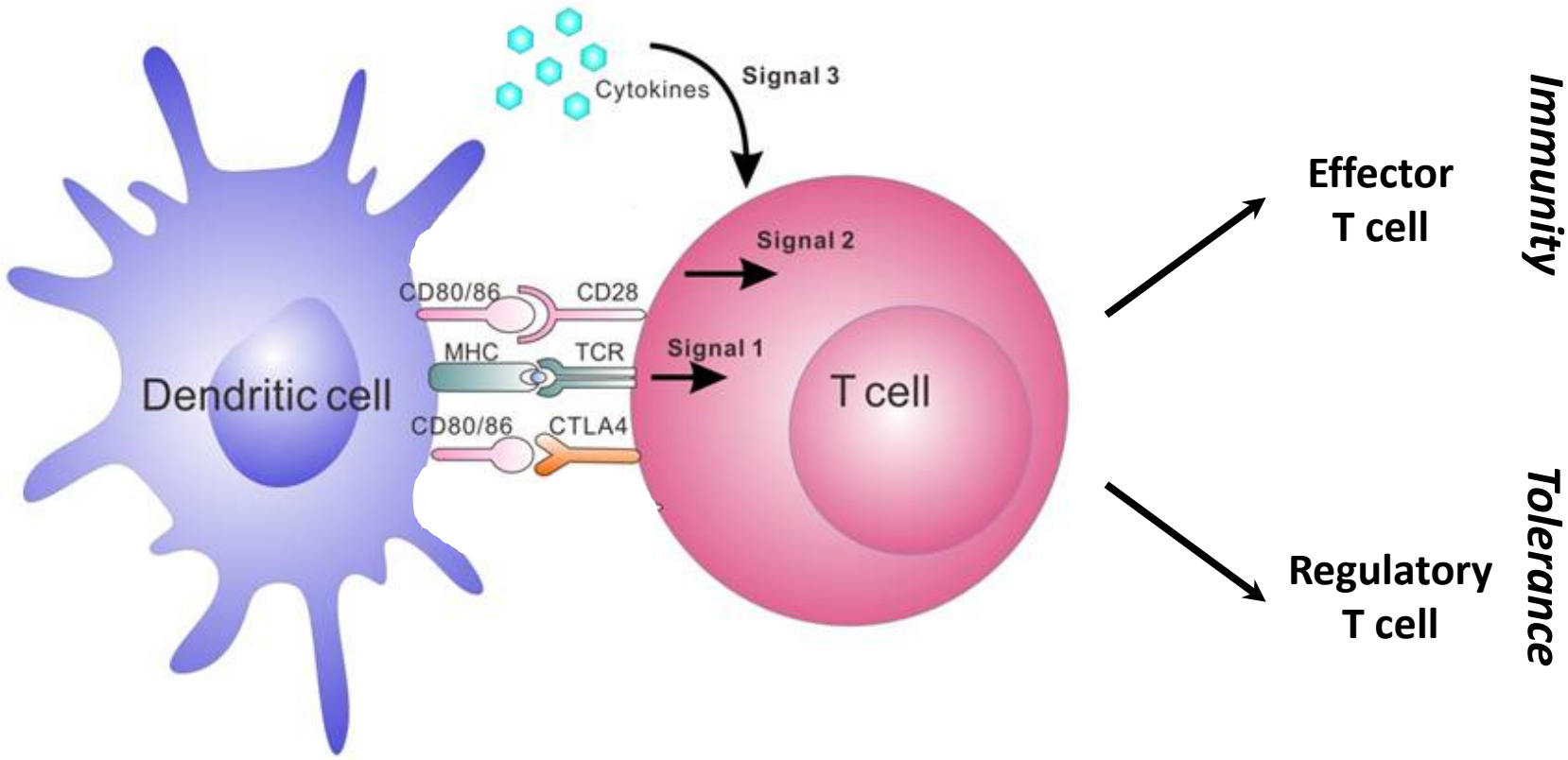
Mark Middleton

Professor of Experimental Cancer Medicine and Head of Department of Oncology at Oxford. Mark has developed an international reputation in the fields of melanoma and early drug development, initiating numerous clinical trials and contributing to the development of established drugs such as Ipilimumab & T-Vec and new biologics, including IMCgp100 & RGT100.

Tim Maughan

Professor of Clinical Oncology, Department of Oncology, Oxford. Tim is a distinguished translational researcher in colorectal cancer, integrating biological principles into the clinic. He is recognized for his ability to deliver innovation into clinical practice and leads several large research consortia, such as S:CORT.

Dendritic Cells Determine the Outcome of All Immune Responses



Fairchild *et al*. (2015) *Regen Med* **10**:275-286

Limitations of Current Technologies

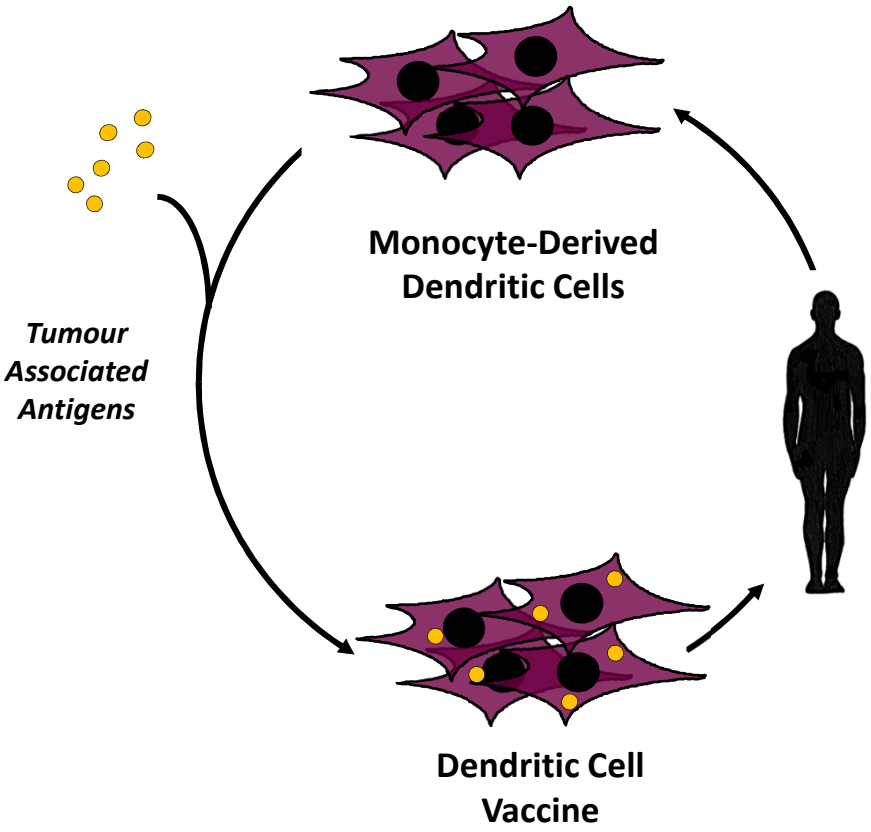
Immune Checkpoint Inhibitors (ICIs)

- ICIs enhance existing immune responses to TAA by disrupting regulatory mechanisms to limit collateral damage to tissues
- Many tumour types, such as uveal melanoma and microsatellite-stable colorectal cancer (MSS-CRC), show poor responses

Autologous CAR-T cells

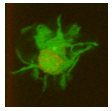
- CAR T cells bypass DCs and the natural mechanisms required to regulate the immune response
- Overshadowed by safety issues caused by off-target effects and may cause long-term immune-compromise of patients
- Currently restricted to cell surface antigens, limiting their application to haematological malignancies and leaving solid tumours with few treatment options

First Generation Dendritic Cell Therapeutics

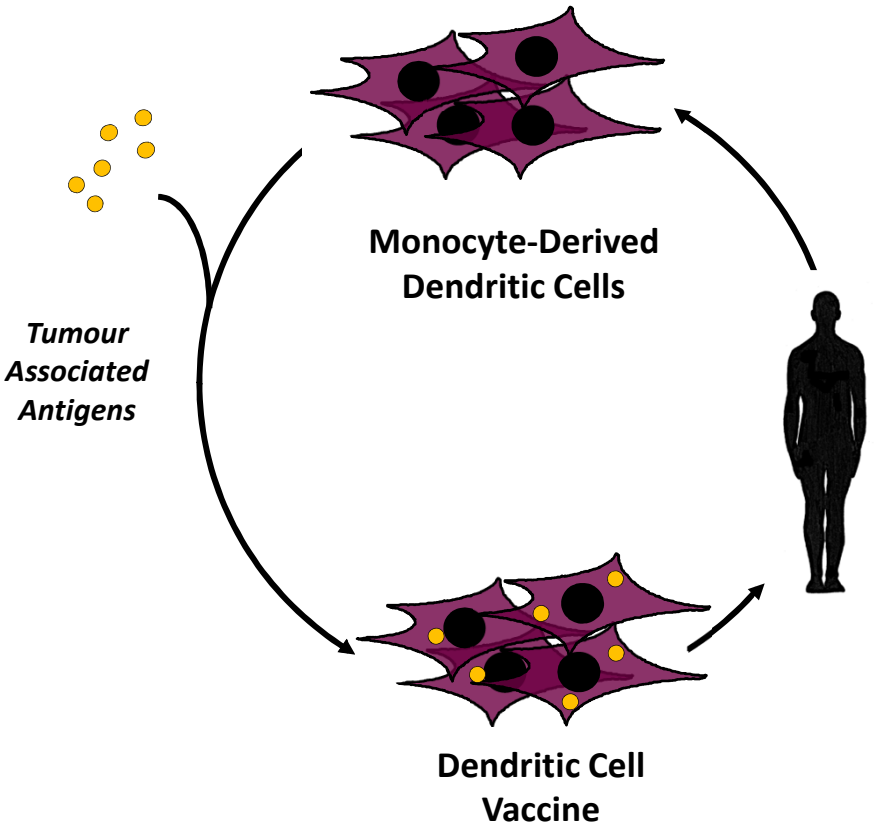


Clinical Trials of Dendritic Cell-Based Vaccines

- More than 200 trials have been conducted in cancer immunotherapy for the treatment of melanoma, prostate cancer, glioblastoma and renal cell carcinoma
- Objective response rates (ORR) in the 8-15% range have typically been reported along with clear evidence of CTL responses in >50% of patients
- Many studies have shown a median prolongation of Overall Survival of ~20%
- Clinical trials over the past two decades have therefore established:
  - DC vaccines are inherently safe and well-tolerated with few adverse events
  - Their administration to patients has a measureable impact on Overall Survival
  - Manufacturing and scale-up under cGMP conditions is entirely feasible
  - A pathway to regulatory approval for adoption by the FDA has been established



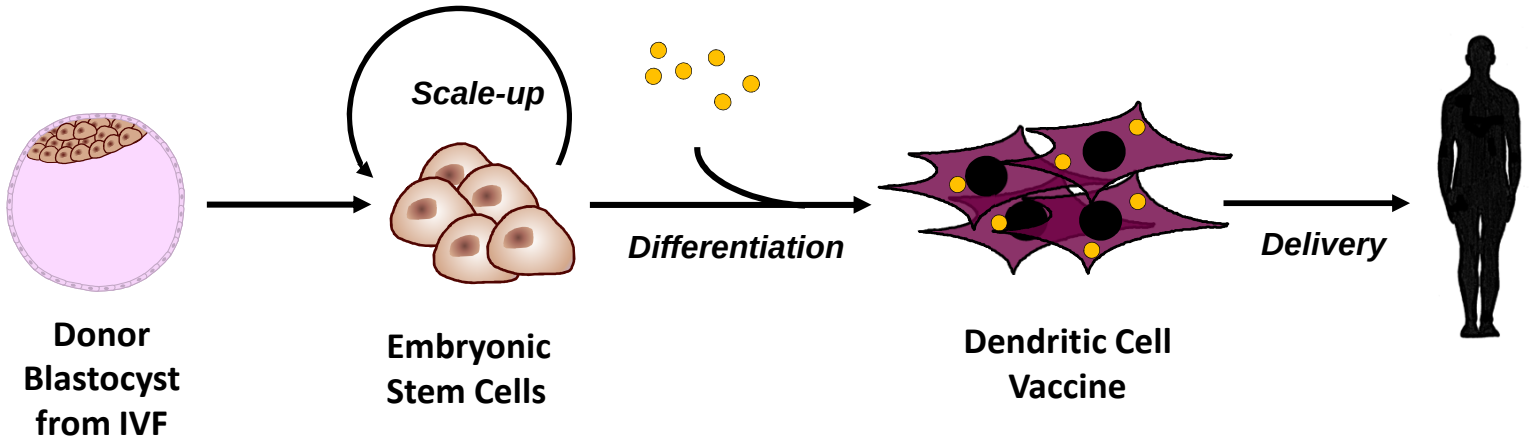
First Generation Dendritic Cell Therapeutics



Limitations of monocyte-derived DC

- Donor-to-donor variation
- Adverse impact of long-term chemotherapy
- Limited capacity to elicit cytotoxic T lymphocyte (CTL) responses

Second Generation Dendritic Cell Therapeutics



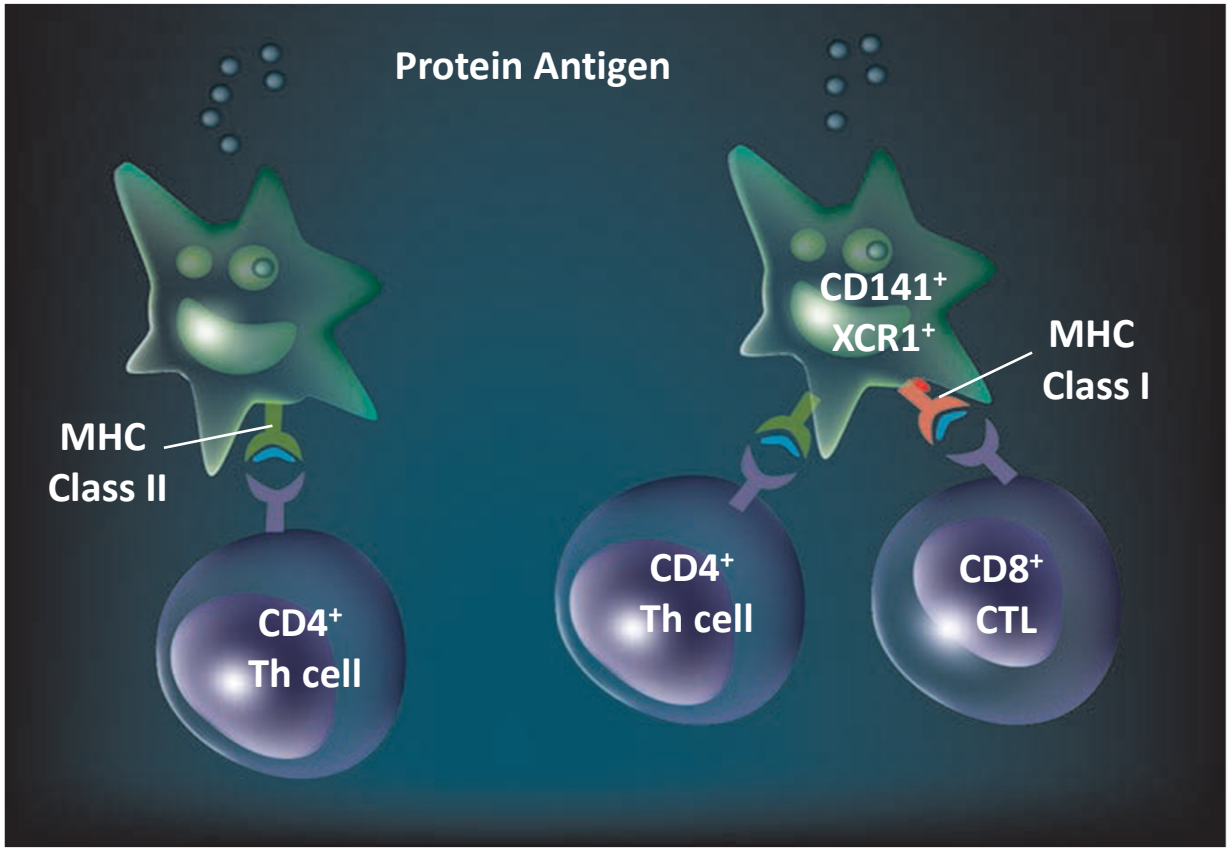
ASTERIAS BIOTHERAPEUTICS

Limitations to the use of ESC-derived DC

- A source of DC allogeneic to the recipient
- Not applicable to tolerance induction
- Limited capacity to elicit CTL responses

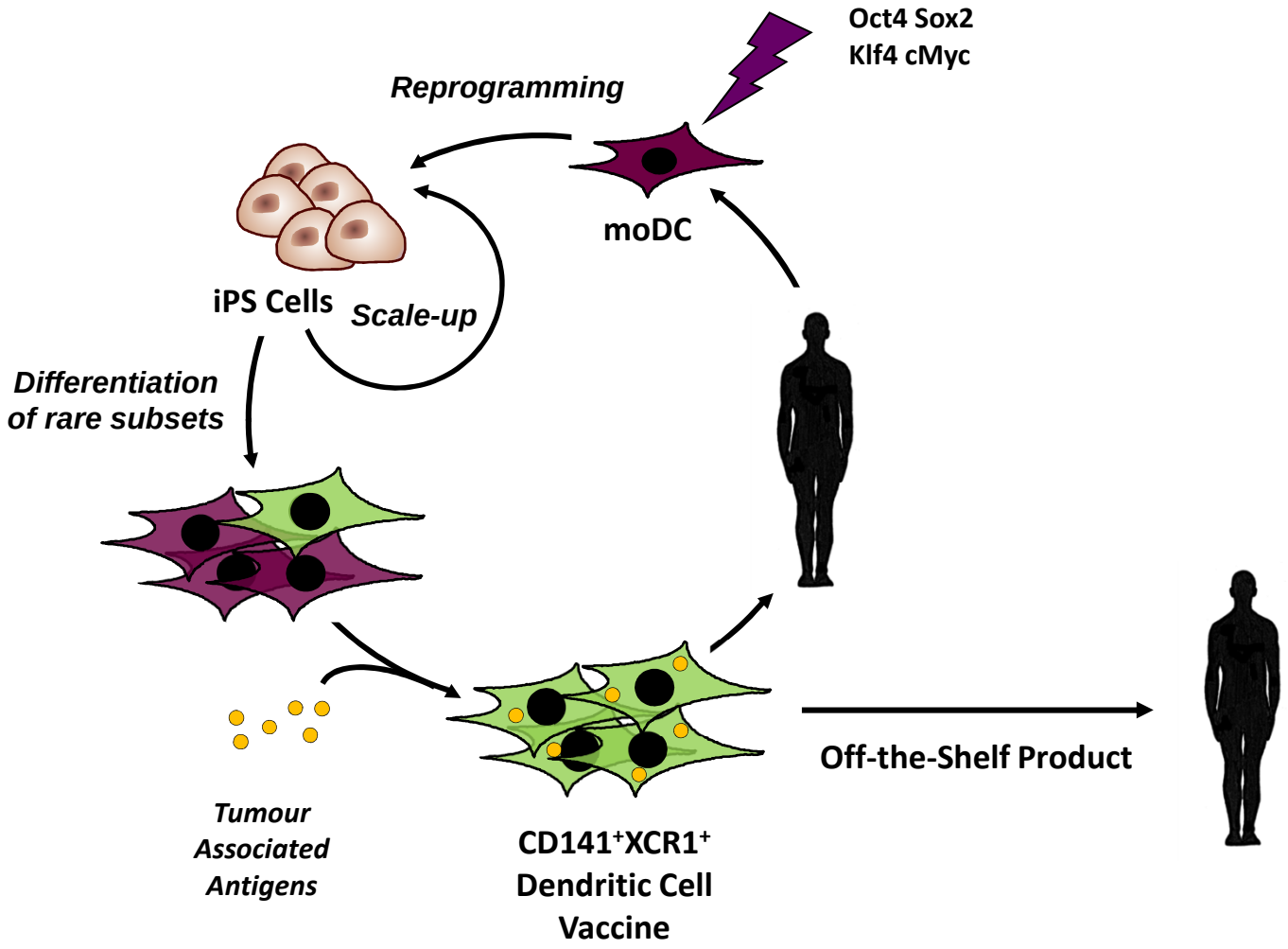
Tseng *et al.* (2009) *Regen Med* **4**:513-526

Antigen Cross-Presentation:
A Requirement for Cancer Immunotherapy

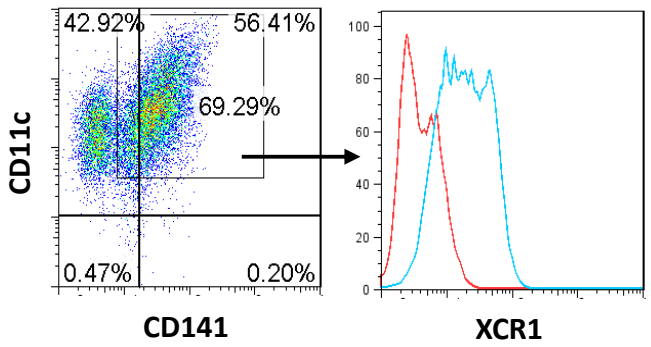


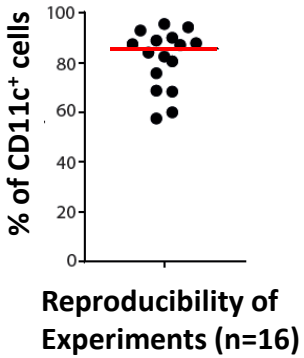
Sachamitr & Fairchild (2012) *Expert Rev Clin Immunol* **8**:547

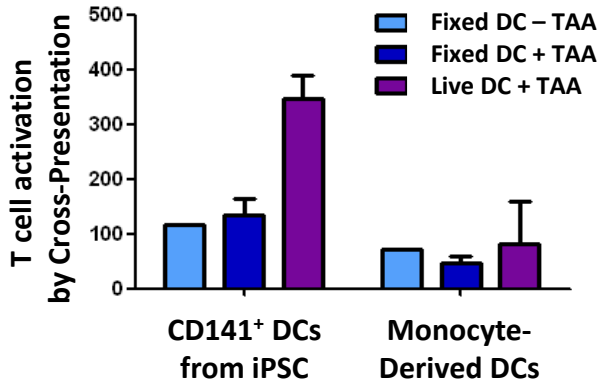
Future Generation Cell Therapy Products

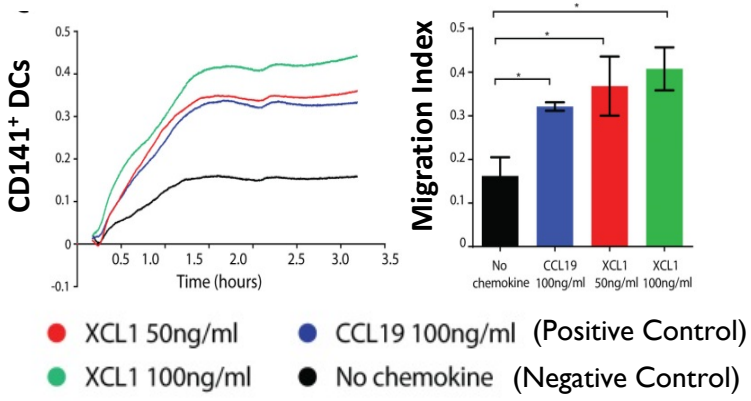


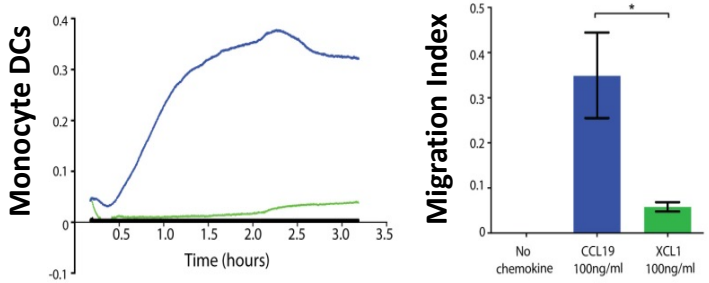
Characterisation of CD141⁺ DC Differentiated from Human iPSC







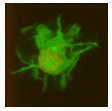




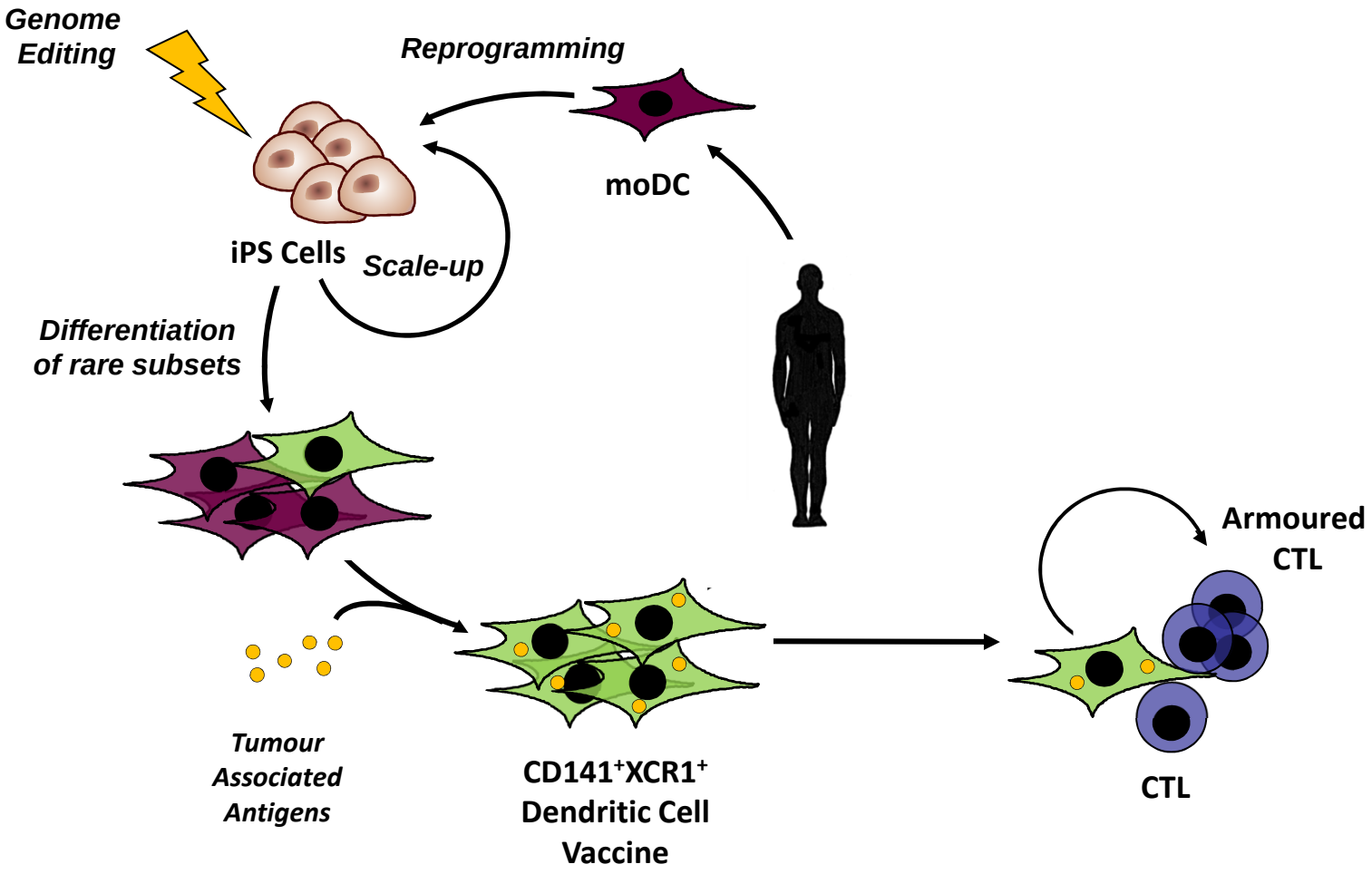
Silk *et al*. (2012) *Gene Therapy* **19**:1035-1040

Strategic Advantages of the OII Dendritic Cell Platform

- The OII platform exploits the cross-presentation capacity of the $CD141^+$ DCs, avoiding the need for transfection or the identification and synthesis of peptide epitopes relevant for each MHC haplotype
- Responsiveness of $CD141^+$ DCs to XCL1 secreted by $CD8^+$ T cells, uniquely directs them towards the very cells capable of responding to TAAs
- Survival of administered DC need only be transient: the legacy of vaccination remains imprinted within the memory T cell repertoire
- Irradiation of the cellular inoculum enhances the safety profile by mitigating against tumorigenesis
- Only modest scale-up in manufacturing is required to produce sufficient numbers
- The platform provides opportunities for future generations of cell therapy products with refined functionality

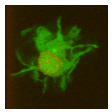


Future Generation Cell Therapy Products



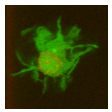
Lead Indication: Low Mutational Burden Cancers

- Despite recent advances in immuno-oncology, the majority of patients fail to respond to ICIs or CAR-T cell therapies, creating a significant unmet medical need
- OII's DC vaccines could play a key role in the treatment of patients bearing tumours with a low mutational burden eg glioblastoma or microsatellite-stable colorectal cancer (MSS-CRC)
- MSS-CRC is the third most common cancer and fourth most common cause of cancer-related deaths worldwide and is predicted to represent a global market of $9.4bn by 2020
- Although many MSS-CRC patients do not respond well to ICIs, they express a number of TAAs: Carcinoembryonic Antigen (CEA) may serve as an appropriate target, either alone or in combination with other known candidates



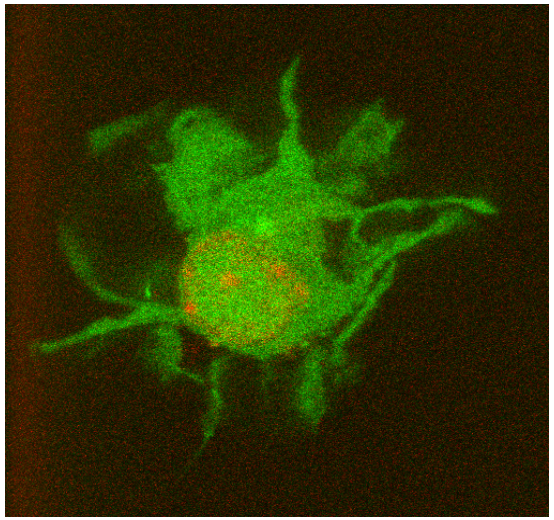
Points of Difference with On-Going Clinical Trials

	First Generation	*Second Generation*	*Next Generation*
	DCVax-L	**AST-VAC2**	**OII-DC**
Source of progenitors	Monocytes	ES cells	**iPS cells**
Autologous	Yes	No	**Yes/No**
Impact of prior chemotherapy	High	None	**Low**
Manufacture may be standardised	No	Yes	**Yes**
Capacity for antigen cross-presentation	No	No	**Yes**
Directed migration towards CTL	No	No	**Yes**
Suitability for tolerance induction	Yes	No	**Yes**



Scope of the OII Intellectual Property

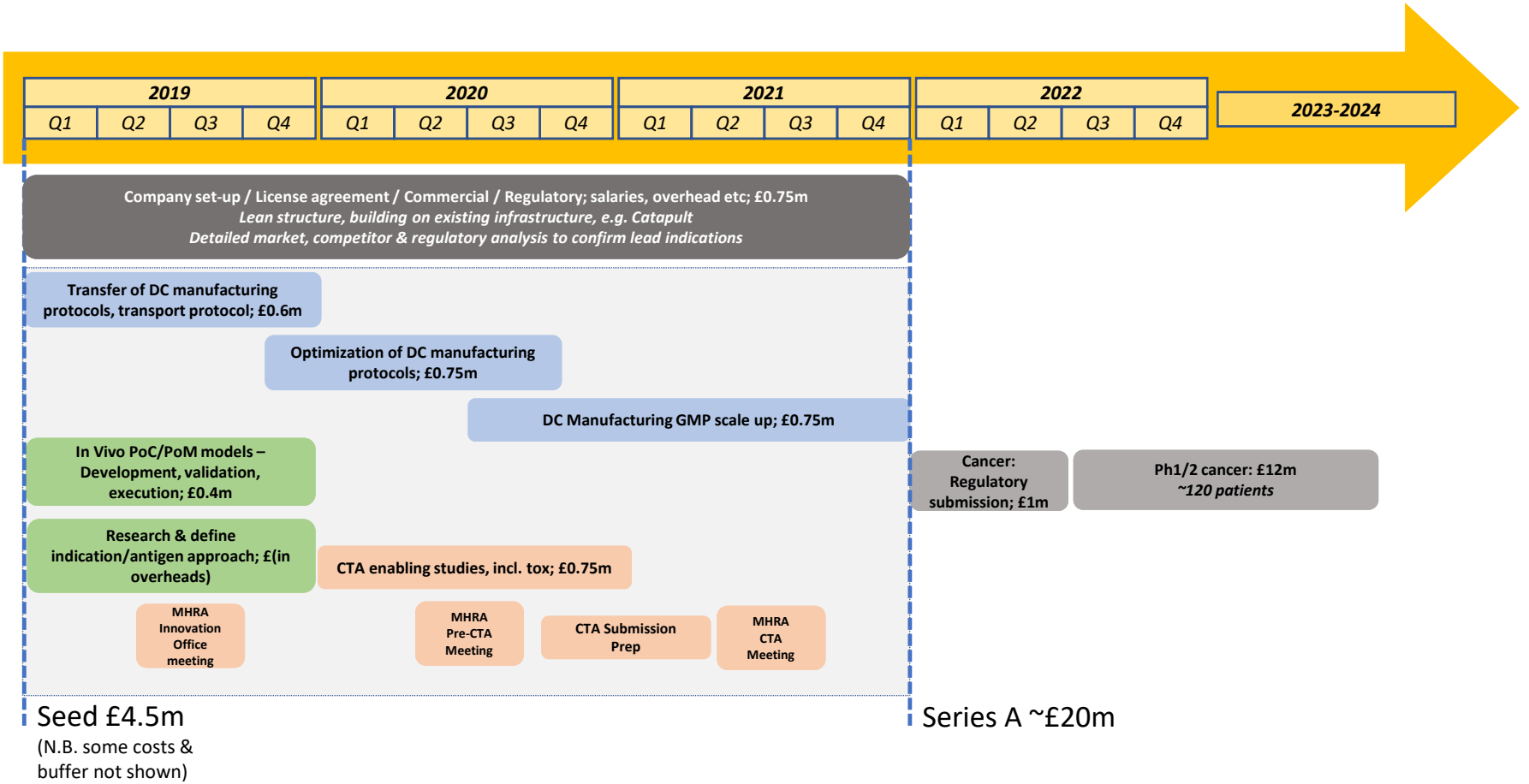
- Differentiation of the CD141^{+} subset of DC with superior capacity to cross present exogenous antigens to T cells for vaccination purposes[1]
- Method for producing iPSCs that predisposes DCs differentiated from them to provoke robust immune responses or silence immunity to establish tolerance[2]
- Identification of novel pluripotency genes capable of enhancing reprogramming efficiency (restricted field)[3]
- OII will further expand its IP portfolio through in-house development and in-licensing



1. PCT/GB2012/050447 Granted in the US & pending in the EU
2. PCT/GB2017/050201 National phase US, Europe & China
3. PCT/GB2017/052217

Initial Programme:

Plan A: Seed round of £4.5m



Initial Programme:

Plan B: Two Tranches Totalling £4.5m