Dendritic Cells: The ‘Sentinels’ of the Immune System

- Dendritic cells (DCs) function as ‘sentinels’ of the immune system: as the most potent antigen-presenting cells, they are responsible for the initiation of all adaptive immune responses.
- DCs are specialised to capture and process antigens, generating peptides that are presented on major histocompatibility complex (MHC) molecules recognised by T cells.
- Cross-presentation of tumour antigens to cytotoxic T lymphocytes (CTLs) may facilitate tumour destruction.

OxVax: Next Generation Dendritic Cell Platform
First Generation DC Vaccines: Autologous Monocyte-Derived DC (moDC)

Limitations of moDC

- Donor-to-donor variation due to adverse impact of long-term chemotherapy
- Limited capacity to elicit CTL responses
- No equivalent population *in vivo?*

What you really want to use is the cDC1 subset but these are inaccessible
Next Generation Dendritic Cell Cancer Vaccine Platform

- Based on **proprietary specialized CD141⁺ dendritic cells DCs**, consistent with the cDC1 subset *in vivo*, in which:
  - co-expression of chemokine receptors CCR7 and XCR1 guides migration toward lymphoid tissues and cytotoxic T cells (CTLs) respectively
  - antigen uptake facilitates cross-presentation of tumour antigens to MHC class I-restricted CTLs
  - epitopes selected by the DCs are appropriate to each individual, circumventing the need for their identification and bespoke manufacture

- Cost effective, **off-the-shelf** product using proprietary iPSC differentiation protocol for **bulk cGMP manufacture**

- Suitable for use early in neoadjuvant/adjuvant treatment across a broad range of cancers
Next Generation Vaccines: CD141$^+$ DCs

- Oct4 Sox2 Klf4 cMyc
- Reprogramming
- moDC
- Scale-up
- iPS Cells
- Differentiation of rare subsets
- Antigen Source
- CD141$^+$XCR1$^+$ Dendritic Cell Vaccine
- Off-the-Shelf Product
- HLA-A2$^+$ Recipient
- HLA-A2$^+$ Donor

OxVax: Next Generation Dendritic Cell Platform
Characterisation and Potency Assays


XCR1

CD11c

CD141

% of CD11c+ cells

Reproducibility of Experiments (n=16)

CD141+ DCs from iPSC

Monocyte-Derived DCs

Migration Index

Fixed DC – TAA

Fixed DC + TAA

Live DC + TAA

Monocyte DCs

CD141+ DCs

(Positive Control)

(Positive Control)

(Positive Control)

(Positive Control)

Also, pilot POC ata show a trend towards dose-dependent antigen-specific CTL activation


OxVax: Next Generation Dendritic Cell Platform
Intellectual Property

• Differentiation of the CD141\(^+\) subset of DCs 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 to tumour antigens\(^2\)
• Identification of novel pluripotency genes capable of enhancing reprogramming efficiency (restricted field)\(^3\)
• OxVax 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 entry July 2018
3. PCT/GB2017/052217
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 and has conducted world leading research at both Oxford and Cambridge Universities that has led to first-in-man clinical trials for the treatment of non-small cell lung cancer. 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. A candidate for the MSc in Experimental Therapeutics, working with Paul on the development of OxVax

Tim Davies

Research scientist with over 35 years’ experience in the field of stem cell biology and immunology. Tim trained at Cardiff University and Birkbeck College, London before joining Sir Richard Gardner’s laboratory at Oxford for which he served as manager for more than 20 years. He has been instrumental in developing the protocols for derivation and differentiation of iPSC, on which the OxVax technology is based

OxVax: Next Generation Dendritic Cell Platform
Investment/Partnering Opportunity

- OxVax is seeking £3m seed funding to establish robust *in vitro* PoC, demonstrate cGMP supply chain capability and clarify pathways to the clinic for its lead indication.
- The company seeks partners interested in accessing the specialized CD141⁺ Dendritic Cell (DC) subset for their own field of application, including other oncology indications or applications of the platform exploiting immunogenicity or the induction of tolerance.