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Tumour arginine addiction subverts the anti-cancer immune response

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Arginine is a semi-essential amino acid whose physiological levels are maintained principally from dietary intake and through intestinal-renal recycling of citrulline. At the cellular level, arginine metabolism is essential for cell division, protein synthesis and as a precursor for nitric oxide and polyamines. The role of arginine processing in the tumour microenvironment to impair anti-tumour immunity has become increasingly apparent. T cells, which provide the corner stone of the anti-cancer immune response, are notably arginine dependent. Tumour associated macrophages (TAMs) and the induction of Myeloid-derived suppressor cells (MDSCs) can decrease local and systemic arginine concentrations, through increased arginase 1 expression, suppressing T cell proliferation. TAM and MDSC derived reactive nitric oxide species production via expression of iNOS, may further inactivate T cell responses. More recently the malignant cells of some haematological and solid tumours have been recognised to be arginine addicted, due to the loss of critical arginine recycling enzymes – a state known as arginine auxotrophism. The resulting dependence on extracellular arginine from the blood and tumour microenvironment further suppresses both antigen-specific and non-specific T cell responses. The importance of these findings and their translational consequences will be presented in this meeting.

Biography

Francis Mussai is a Senior Clinical Lecturer at the University of Birmingham, UK and leads a research group investigating the immunosuppressive microenvironment created by both paediatric and adult malignancies. The group has identified key aspects of how arginine catabolism by both tumour cells and tumour associated myeloid cells can alter anti-cancer immunity. He is also a Consultant Paediatric Oncologist and is involved in the development of early phase clinical trials for paediatric malignancies in the UK and Europe.

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