

# The dual role of inflammation in cancer immunity



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### **Abstract**

Immunotherapy constitutes the most promising pan-cancer treatment approach since the development of the first chemotherapies. Unprecedented outcomes continue to be observed in multiple cancer types including malignancies once thought treatment refractory. Responses, especially complete and durable, are nevertheless only observed in a limited fraction of patients underscoring the need for basic research to elucidate the basis for these remarkable but rare outcomes. Our group at the Cancer Research UK Manchester Institute investigates the principles that regulate the establishment of tumour microenvironments that support or restrain cancer progression spontaneously or following treatment. Combining the use of genetically engineered pre-clinical models with the analysis of cancer patient samples we aim to identify the underlying mechanisms that allow immune escape and enable progressive tumour growth. In doing so, we have identified the cyclooxygenase (COX)-2/prostaglandin E<sub>2</sub> (PGE<sub>2</sub>) pathway as a nodal inflammatory axis that drives immune evasion and therapy resistance. Of therapeutic relevance, we showed that pharmacological inhibition of the COX-2/PGE<sub>2</sub> pathway with widely used anti-inflammatory drugs represents a promising approach to augment the efficacy of immunotherapy and chemoimmunotherapy combinations. Collectively, our data uncovers the COX-2/PGE<sub>2</sub> axis as a *bona fide* immune checkpoint that can be readily targeted to enhance the efficacy of immune-based cancer treatments.

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### **Biography**

Dr Santiago Zelenay obtained his biology degree from the University of Buenos Aires in 2002 where he worked on DNA vaccines. He then undertook his PhD in Immunology at the Institute Gulbenkian of Science studying the origin and function of regulatory T cells. In 2008, he joined the CRUK London Research Institute/Francis Crick Institute, where he investigated innate immune receptors and signaling pathways that trigger dendritic cell activation and drive T cell responses against viruses or tumours. In 2015, Santiago joined the CRUK Manchester Institute where he is senior group leader of the Cancer Inflammation and Immunity group. In 2017, he received the CRUK Future Leaders in Cancer Research Prize and in 2019, together with co-authors, he was awarded the BIAL Award in Biomedicine for the study Zelenay et al, *Cell* 2015.