## Intra-tumoural nitric oxide release by macrophages activated by Gc-protein-derived Macrophage Activating Factor (GcMAF)

Marco Ruggiero<sup>1,3</sup>, Massimo Gulisano<sup>2</sup>, <u>Jacopo J.V. Branca</u><sup>2</sup>, Gabriele Morucci<sup>2</sup>, David Noakes<sup>3</sup>, Stefania Pacini<sup>2</sup>

Over past decades, nitric oxide (NO) has emerged as a molecule of interest in cancer treatment because of its tumouricidal properties (Choudhari et al., 2013). Gc-protein-derived Macrophage Activating Factor (GcMAF) induces the synthesis and release of NO by activated macrophages. It was previously demonstrated that molecular complexes of oleic acid (OA) and GcMAF (OA-GcMAF) stimulate macrophage activation in cancer patients (Ward et al., 2014). Here we demonstrate that intratumoural injection of OA-GcMAF leads NO synthesis and release inside the tumour. Under ultrasound guidance, OA-GcMAF was injected into patients harbouring different types of solid tumours; a metastasis from a melanoma, and a metastasis from breast cancer. Intra-tumoural NO synthesis and release was monitored in real-time by power-doppler ultrasonography. One to two minutes after injection, we observed a significant increase in blood flow and in blood vessels diameter, a clear indication of vasodilation due to NO synthesis and release. These observations substantiate the dramatic clinical results previously observed by Ward et al. (2014), and open the way to further investigation in the role of GcMAF as a powerful anticancer agent.

## References

1]	Choudari et al.	(2013	) Nitric oxic	le anc	l cancer: a review. World	I Surg Onco	ol 11: 118-129

[2] Ward et al. (2014) Clinical Experience of Cancer Immunotherapy integrated with Oleic Acid Complexed with De-glycosylated Vitamin D Binding Protein. Am J Immunol 10: 23-32.

Keywords		
Reywords		

Nitric Oxide, GcMAF, immunotherapy, breast cancer, ultrasonography.

<sup>&</sup>lt;sup>1</sup> Department of Experimental and Clinical Biomedical Sciences, University of Firenze, 50134 Firenze, Italy

<sup>&</sup>lt;sup>2</sup> Department of Experimental and Clinical Medicine, University of Firenze, 50134 Firenze, Italy

<sup>&</sup>lt;sup>3</sup> Immuno Biotech Ltd; GY1 6NB Guernsey, Channel Islands, UK