

**Project title:** Antibody-based immunomodulation in hepatocellular carcinoma

**PI:** Prof. Lucia Anna Stivala

**Hosting laboratory:** Department of Molecular Medicine, Unit of Immunology and General Pathology

**Background:** Liver cancer is the third leading cause of cancer death and the sixth most common cancer globally. Hepatocellular carcinoma (HCC) is the most common type of liver cancer and is linked to chronic liver diseases such as viral infection, diabetes, and obesity making it an increasingly common cancer in Western countries where it is related to alcohol use, metabolic diseases, non-alcoholic fatty liver disease (NAFLD), cirrhosis, and aging related genetic abnormalities. Moreover, HCC is frequently diagnosed at an advanced stage due to the lack of early symptoms and although progress is being made in treatment with targeted therapies and most recently immunotherapies, the prognosis for HCC remains poor.

One of the most promising therapeutic approaches in oncology has been based on the recognition of the role of our immune system in controlling cancer. This understanding has given us an important new tool: harnessing a patient's immune system to fight cancer.

**Approach:** Our laboratory has a long history of working on oncogenes and the development of blocking antibodies and inhibitors (1, 2, 3) and has shifted focus to immune modulation and the tumour microenvironment in HCC and other solid tumours. The proposed PhD project involves the development of several functional antibodies to specific tumour antigens among which MICA/B, CD155, TGF $\beta$ , and c-MET. The antibodies will be used for the specific modulation of tumour infiltrating immune cells (i.e. T-cells, NK-cells, and macrophages) and the targeted blocking of immune-suppressive signals originating from tumour cells and associated mesenchymal cells (such as fibroblasts) in the tumour microenvironment. We are currently also combining these antibodies with Chimeric Antigen Receptor (CAR) technology in close collaboration with the laboratory of Dr Rio Sugimura at the University of Hong Kong.

**We are looking for:** a highly-motivated candidate with a strong background in cell biology and biochemistry and an interest in acquiring a wide range of new skills through collaborations with other laboratories. Research activities abroad are likely to occur and offer an opportunity to broaden the candidate's horizon.

**For more information,** please contact Prof. Lucia Anna Stivala @ [luciaanna.stivala@unipv.it](mailto:luciaanna.stivala@unipv.it)

**Bibliography:**

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3. DiCara, D. M. et al. Characterization and structural determination of a new anti-MET function-blocking antibody with binding epitope distinct from the ligand binding domain. *Sci Rep-uk* 7, 9000 (2017).

