ImmunoTools *special* Award 2017

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Defining the immune microenvironment cartography of Pituitary tumours to improve immunotherapies

Pituitary tumours are the second most common intracranial neoplasms, comprising 10-15% of diagnosed brain tumours. Predicting pituitary tumour behaviour remains a challenge as those tumours present various characteristics based on their hormonal expression (Prolactin, ACTH, GH, FSH, LH and TSH) and their secretory capability (functioning or non-functioning lesions)[1]. Among those tumours, a subset of pituitary adenomas exhibits an aggressive clinical course and patients recur despite surgery, radiation and chemotherapy[2]. There is therefore a need to develop new therapeutics.

Apart from tumour cells themselves, other cell-types are recruited and corrupted by the transformed cells. The interactions between cancer and non-cancer cells define the tumour microenvironment (TME). Surprisingly, the non-malignant cells of the TME can comprise >50% of tumour mass including infiltrated immune cells, cancer associated fibroblasts (CAF) and the tumour vasculature. While the existence of TME is well accepted & described in numerous cancers such a Breast and Pancreatic cancers, little is known about the Pituitary TME. Interestingly, some recent reports published in 2015, highlight the existence of Tumour infiltrating Lymphocytes (TiLs)[3-4], Tumour-associated Macrophages (TAM)[4] and progenitor mesenchymal cells (PMCs)[5-6] in Pituitary tumours. Moreover, the presence of CD45 positive infiltrating-cells has been associated with a poor clinical post-surgery outcome among 25% of patients with Pituitary adenomas[7]. These results support that the TME of pituitary cancer could have a major function and impact on the progression of these tumours, yet these aspects are currently poorly understood.

The aim of our project is to provide a precise characterization of human Pituitary Tumours TME, with a dedicated focus on immune populations. Our access to a large number of fresh resected human Pituitary Adenoma as well as blood sample of matching patients as already been granted thanks to the collaboration with an oncologist and a neurosurgeon. They will provide access to a large number of fresh

resected samples, estimated at 100 cases of adenomas from different hormonal origin resected per year. Technical approach to dissociate tumour prior their phenotyping on Flow cytofluorimeter (18 colours) and their subsequent analyses with specific software have already been validated on a cohort of 10 resected pituitary tumours.

The ImmunoTools flow cytometry antibodies selected below will be essential for our ambitious and challenging project to better understand and characterize the immune mechanisms involved in Pituitary tumours. These reagents should further help to define a precise cartography of the immune-populations that exist in each analysed patients. This work will further help to determine the immune-signature of the different subset of Pituitary adenomas we will analysed (Prolactinomas, Corticotroph-, Gonadotroph- and Somatotroph- tumors).

References:

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ImmunoTools *special* AWARD for **Moitza Principe** includes 25 reagents

anti-human antibodies for flow cytometry:

FITC - conjugated anti-human CD3, CD4, CD45, HLA-DR.

PE - conjugated anti-human CD14, CD19, CD34, CD44, CD105, IFN-gamma, TNFa.

PerCP - conjugated anti-human CD3, CD45.

APC - conjugated anti-human CD8, CD9, CD11b, CD25, CD31, CD56, Annexin V.

recombinant human cytokines:

rh BMP-2, rh BMP-7, rh IL-2, rh Myostatin, rh TGF-beta3. DETAILS more AWARDS