

Histological and transcriptomic cartography identify S100B-FolliculoStem cells as a candidate signalling hub that may drive pituitary tumour behaviour.

***Mirela D ILIE*^{1,2}, *Maxime LEPETIT*³, *Marie CHANAL*¹, *Hector HERNANDEZ-VARGAS*¹, *Alexandre VASILJEVIC*^{1,4}, *Nicolas GADOT*⁵, *Laura CHINEZU*⁶, *Emmanuel JOUANNEAU*^{1,7}, *Gerald RAVEROT*^{1,8}, *Olivier GANDRILLON*³, *Franck PICARD*³, *Philippe BERTOLINO*¹**

1- Inserm U1052, CNRS UMR5286, University Claude Bernard Lyon 1, Cancer Research Center of Lyon, Lyon, France

2- Endocrinology Department, “C.I. Parhon” National Institute of Endocrinology, Bucharest, Romania

3- Laboratoire de Biologie et Modélisation de la Cellule, ENSL, 46 allée d’Italie, 69364 LYON, FRANCE

4- Pathology Department, Reference Center for Rare Pituitary Diseases HYPO, Groupement Hospitalier Est Hospices Civils de Lyon, Bron, France.

5- Pathology Research Platform, Department of Translational Research and Innovation, Centre Leon Berard, Lyon, France

6- Pathology Department, Targu Mures Emergency Hospital, Targu Mures, Romania

7- Neurosurgery Department, Reference Center for Rare Pituitary Diseases HYPO, “Groupement Hospitalier Est” Hospices Civils de Lyon, Bron, France

8- Endocrinology Department, Reference Center for Rare Pituitary Diseases HYPO, Groupement Hospitalier Est” Hospices Civils de Lyon, Bron, France

Pituitary tumours (PitNETs) are frequent neoplasms derived from endocrine cells of the anterior pituitary gland. While mainly benign their aggressive course are frequently associated with important comorbidities. PitNETs heterogeneity and behaviour are poorly understood, which result in a limited number of available therapeutic options beside surgery and radiotherapies.

Similar to other cancers, understanding the intricate exchanges that exist between tumour cells and their microenvironment represents a goal to improve our understanding of the pituitary tumour biology beyond genetics. It constitutes therefore an important tool for developing future therapies.

Taking advantage of recent technical advances in high throughput imaging, single cell RNAseq and spatial transcriptomics, we addressed the spatial distribution and role of S100B+ Folliculostellate cells, a non-endocrine resident cells, found in normal pituitary and gonadotroph tumours.

Taken together, our work support the presence of those cells in gonadotroph tumours and their role as a signalling hub. Further studies are now required to: 1) determine whether their spatial location drive a functional remodelling of tumours, 2) infer their signalling network and 3) fully comprehend their implication in pituitary tumours as a signalling hub or a tumour fuelling population.