

EYES Research and Clinical Observership Programme (C.O.P./R.O.P)
La Conception and La Timone Hospital, Marseille, France
Marseille Medical Genetics, Aix Marseille University, Marseille, France

The Department of Endocrinology at La Conception Hospital in Marseille, France, is the coordinating center of the French Reference Center for Rare Pituitary Diseases (HYPO). The department manages a large number of patients with pituitary diseases, including tumors, inflammatory diseases, and deficiencies. The department has strong connections with several other clinical departments, including neurosurgery, radiotherapy, endocrine pediatrics, and endocrine surgery, as well as molecular biology. Some topics of interest to the clinical department are strongly interconnected with basic research in the MOPED (Mechanisms of Paracrine and Endocrine Disorders) team at the Marseille Medical Genetics Unit (INSERM, Aix-Marseille University), led by Prof. Anne Barlier, Head of the Molecular Biology Department.

The clinical team includes seven full-time MDs (three of whom have Ph.D.s and one who is a Ph.D. candidate), seven to eight residents, and seven to eight medical students. The department has welcomed foreign students and MDs from around the world.

Clinical Activities/Research Topics of Interest

The department's activities focus on general endocrinology, with the exception of diabetes, nutrition, and obesity, as well as rare diseases in all fields of endocrinology. More specifically, the department is interested in

- Pituitary and adrenal tumors
- Therapeutic education, especially for hormone deficiency
- Graves' orbitopathy
- Bone and calcium metabolism
- PCOS and endocrine gynecology
- Endocrine side effects of immune checkpoint inhibitors

Over the last ten years, these topics have resulted in over 300 publications. We regularly consider and discuss innovative ways to diagnose and treat these patients. The department is also conducting several industry-sponsored protocols (phases II, and III) together with two dedicated clinical research platforms and several ongoing prospective and retrospective evaluations of our large patient cohorts.

Apart from taking part in our regular multidisciplinary board meetings, other activities such as systematic reviews, retrospective studies, or longer-term prospective collaborative studies (participate or initiate) on these topics can be considered during the time of presence.

Topics of Interest in Basic Research

The research unit's activities focus on the use of induced pluripotent stem cells that have been differentiated into mature pituitary cells. Initially, this work aimed to better understand the mechanisms and roles of some transcription factors/pathways during pituitary development. Our team is one of the few worldwide with a protocol allowing these differentiation steps. Current work aims to improve these techniques and use them as a model to better understand pituitary tumorigenesis. Apart from participating in the weekly research meetings and seminars of the Marseille Medical Genetics team, the applicant's role would mainly be observational in collaboration with the molecular biology department. Collaboration on a Ph.D. thesis, either clinical or basic, can be discussed during the applicant's time here.

Contact person

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- ROP : Anne Barlier, Head of the basic research team, MD, Ph.D ; Head of the molecular biology department - Anne.barlier@univ-amu.fr

Early career investigators

- Nicolas Sahakian, MD, Ph.D candidate - Nicolas.sahakian@ap-hm.fr
- Cecilia Piazzola, MD, Ph.D candidate - Cecilia.piazzol@ap-hm.fr

Specific Rules and Regulations

Depending on the applicant's country, the regulatory process may be conducted with either the hospital (AP-HM) or Aix-Marseille University. Each entity has its own specific approval rules. French proficiency would make it easier to participate in clinics and outpatient clinics. However, this is not mandatory, and depending on the applicant's wishes, the profile of activities can be modified (for instance, mixed clinical and basic research activities for English-speaking applicants might also be possible to have a global overview of our activities).

Selection of 20 publications of interest (2021-2025)

Cushing and adrenals

- 1: Piazzola C, Graillon T, Girard N, Dufour H, Brue T, Castinetti F. Desmopressin is a safe and effective secretagogue to replace corticotropin- releasing hormone in petrosal sinus sampling. *Ann Endocrinol (Paris)*. 2025 Apr;86(2):101678. doi: 10.1016/j.ando.2024.101678. Epub 2024 Dec 19. PMID: 39709151.
- 2: Piazzola C, Dreves B, Albarel F, Nakache J, Morera J, Joubert M, Brue T, Reznik Y, Castinetti F. Plasma Renin: A Useful Marker for Mineralocorticoid Adjustment in Patients With Primary Adrenal Insufficiency. *J Endocr Soc*. 2024 Oct 11;8(11):bvae174. doi: 10.1210/jendso/bvae174. PMID: 39416427; PMCID: PMC11481017.
- 3: Amodru V, Ferriere A, Tabarin A, Castinetti F, Tsagarakis S, Toth M, Feelders RA, Webb SM, Reincke M, Netea-Maier R, Kastelan D, Elenkova A, Maiter D, Ragnarsson O, Santos A, Valassi E; and for the ERCUSYN Study Group. Cushing's syndrome in the elderly: data from the European Registry on Cushing's syndrome. *Eur J Endocrinol*. 2023 Apr 5;188(4):395-406. doi: 10.1093/ajendo/lvad008. PMID: 36749009.
- 4: Castinetti F, De Fremerville JB, Guerin C, Cornu E, Sarlon G, Amar L. Controversies about the systematic preoperative pharmacological treatment before pheochromocytoma or paraganglioma surgery. *Eur J Endocrinol*. 2022 Mar 18;186(5):D17-D24. doi: 10.1530/EJE-21-0692. PMID: 35230260.
- 5: Hochman C, Cristante J, Geslot A, Salenave S, Sonnet E, Briet C, Bachelot A, Chevalier N, Gilly O, Brue T, Hadjadj S, Kerlan V, Chanson P, Vezzosi D, Chabre O, Drui D, Castinetti F. Pre-term birth in women exposed to Cushing's disease: the baby-cush study. *Eur J Endocrinol*. 2021 Mar;184(3):469-476. doi: 10.1530/EJE-20-1224. PMID: 33486470.
- 6: Jullien N, Saveanu A, Vergier J, Marquant E, Quentien MH, Castinetti F, Galon-Faure N, Brauner R, Marrakchi Turki Z, Tauber M, El Kholy M, Linglart A, Rodien P, Fedala NS, Bergada I, Cortet-Rudelli C, Polak M, Nicolino M, Stuckens C, Barlier A, Brue T, Reynaud R; Genhypopit Network. Clinical lessons learned in constitutional hypopituitarism from two decades of experience in a large international cohort. *Clin Endocrinol (Oxf)*. 2021 Feb;94(2):277-289. doi: 10.1111/cen.14355. Epub 2020 Dec 21. PMID: 33098107.

Genetics and Basic research

- 1: Brandi ML, Pieterman CRC, English KA, Lines KE, Shariq OA, Marini F, Cuny T, Lewis MA, Stratakis CA, Perrier ND, Waguespack SG, Castinetti F, Valk GD, Thakker RV; Delphi Expert Panel. Multiple endocrine neoplasia type 1 (MEN1): recommendations and guidelines for best practice. *Lancet Diabetes Endocrinol*. 2025 Aug;13(8):699-721. doi: 10.1016/S2213-8587(25)00119-6. Epub 2025 Jun 13.
- 2: Mac TT, Fauquier T, Jullien N, Romanet P, Etchevers H, Barlier A, Castinetti F, Brue T. Modeling corticotroph deficiency with pituitary organoids supports the functional role of *NFKB2* in human pituitary differentiation. *Elife*. 2024 Nov 28;12:RP90875. doi: 10.7554/eLife.90875. PMID: 39607428; PMCID: PMC11604219.

- 3: Fourneaux R, Reynaud R, Mougel G, Castets S, Bretones P, Dauriat B, Edouard T, Raverot G, Barlier A, Brue T, Castinetti F, Saveanu A. IGSF1 mutations are the most frequent genetic aetiology of thyrotropin deficiency. *Eur J Endocrinol*. 2022 Nov 3;187(6):787-795. doi: 10.1530/EJE-22-0520. PMID: 36201163.
- 4: Boukerrouni A, Cuny T, Anjou T, Raingeard I, Ferrière A, Grunenwald S, Maïza JC, Marquant E, Sahakian N, Fodil-Cherif S, Salle L, Niccoli P, Randrianaivo H, Sonnet E, Chevalier N, Thuillier P, Vezzosi D, Reynaud R, Dufour H, Brue T, Tabarin A, Delemer B, Kerlan V, Castinetti F, Barlier A, Romanet P. Genetic testing in prolactinomas: a cohort study. *Eur J Endocrinol*. 2023 Dec 6;189(6):567-574. doi: 10.1093/ajendo/lvad148. PMID: 37956455.

Pituitary disorders

- 1: Miquel L, Testud B, Albarel F, Sahakian N, Cuny T, Graillon T, Brue T, Dufour H, Schleinitz N, Kaplanski G, Ebbo M, Castinetti F. Deciphering the Presentation and Etiologies of Hypophysitis Highlights the Need for Repeated Systematical Investigation. *J Clin Endocrinol Metab*. 2025 May 19;110(6):e1767-e1775. doi: 10.1210/clinem/dgae664. PMID: 39312231.
- 2: Sahakian N, Goetz L, Appay R, Graillon T, Raingeard I, Piazzola C, Regis J, Castinetti F, Brue T, Dufour H, Cuny T. Outcome of non-functioning ACTH pituitary tumors: silent does not mean indolent. *Pituitary*. 2024 Oct;27(5):644-653. doi: 10.1007/s11102-024-01428-6. Epub 2024 Jul 12. PMID: 38995473.
- 3: Amodru V, Sahakian N, Piazzola C, Appay R, Graillon T, Cuny T, Morange I, Albarel F, Vermalle M, Regis J, Dufour H, Brue T, Castinetti F. Changes in multi-modality management of acromegaly in a tertiary centre over 2 decades. *Pituitary*. 2024 Jun;27(3):294-302. doi: 10.1007/s11102-024-01387-y. Epub 2024 Mar 23. PMID: 38521837.
- 4: Sahakian N, Appay R, Resseguier N, Graillon T, Piazzola C, Laure C, Figarella-Branger D, Régis J, Castinetti F, Brue T, Dufour H, Cuny T. Real-life clinical impact of a five-tiered classification of pituitary tumors. *Eur J Endocrinol*. 2022 Nov 29;187(6):893-904. doi: 10.1530/EJE-22-0812. PMID: 36315463.
- 5: Albarel F, Cuny T, Graillon T, Dufour H, Brue T, Castinetti F. Preoperative Medical Treatment for Patients With Acromegaly: Yes or No? *J Endocr Soc*. 2022 Aug 4;6(9):bvac114. doi: 10.1210/jendso/bvac114. PMID: 35965944; PMCID: PMC9368018.
- 6: Castinetti F, Caron P, Raingeard I, Amodru V, Albarel F, Morange I, Chanson P, Calvo J, Graillon T, Baumstarck K, Dufour H, Regis J, Brue T. Lack of delayed neurocognitive side effects of Gamma Knife radiosurgery in acromegaly: the Later-Ac study. *Eur J Endocrinol*. 2021 Nov 30;186(1):37-44. doi: 10.1530/EJE-21-0826. PMID: 34714763.
- 7: Fourneaux R, Vermalle M, Albarel F, Morange I, Graillon T, Amodru V, Cuny T, Dufour H, Brue T, Castinetti F. Acromegaly in remission: a view from the partner. *Eur J Endocrinol*. 2021 Oct 21;185(6):K19-K23. doi: 10.1530/EJE-21-0537. PMID: 34586080.
- 8: Albarel F, Pellegrini I, Rahabi H, Baccou C, Gonin L, Rochette C, Vermalle M, Cuny T, Castinetti F, Brue T. Evaluation of an individualized education program in pituitary diseases: a pilot study. *Eur J Endocrinol*. 2020 Dec;183(6):551-559. doi: 10.1530/EJE-20-0652. PMID: 33055299.

Immune checkpoint inhibitors

- 1: Beaufils M, Amodru V, Tejeda M, Boher JM, Zemmour C, Chanez B, Chrétien AS, Gorvel L, Gravis G, Bruyat D, Mari R, Madroszyk A, Cuny T, Gonçalves A, Lisberg AE, Olive D, Tassy L, Castinetti F, Rochigneux P. Dysthyroidism during immune checkpoint inhibitors is associated with improved overall survival in adult cancers: data mining of 1385 electronic patient records. *J Immunother Cancer*. 2023 Aug;11(8):e006786. doi: 10.1136/jitc-2023-006786. PMID: 37536938; PMCID: PMC10401250.
- 2: Husebye ES, Castinetti F, Criseno S, Curigliano G, Decallonne B, Fleseriu M, Higham CE, Lupi I, Paschou SA, Toth M, van der Kooij M, Dekkers OM. Endocrine- related adverse conditions in patients receiving immune checkpoint inhibition: an ESE clinical practice guideline. *Eur J Endocrinol*. 2022 Oct 25;187(6):G1-G21. doi: 10.1530/EJE-22-0689. PMID: 36149449; PMCID: PMC9641795.