Precision Medicine for rare brain white matter disorders at the Neurometabolic Diseases Lab, IDIBELL, Barcelona, Spain

Brief description of the "Clinical Center" or "Services on undiagnosed rare diseases"

The lab is lead by Aurora Pujol, MD, PhD, FACMG.

Currently integrated by 12 scientists including bioinformaticians, molecular and cellular biologists, biochemists and neurologists, and operates as a reference center in Spain. Our main activities are:

i) Systems neurobiology using Integrative analysis of –omics, to dissect molecular pathogenesis, and tailored treatments;

ii) Clinical genomics for diagnosis, novel gene identification and functional analysis.

We have diagnosed 100 cases per year, with a diagnostic rate of 50%. We developed our prioritisation algorithms and we can provide functional expertise on metabolism, autophagy, ER stress and redox homeostasis.

We are integrated in the URDC at https://www.urdcat.cat/ http://www.neurometabolic-lab.org; https://www.ncbi.nlm.nih.gov/pubmed/?term=Aurora+Pujol

Past (six months) and future/upcoming events related to undiagnosed rare disease

- Efficacy of Network-Based Computational Strategies in the Diagnosis and Novel Gene Identification for Inherited White Matter Disorders. Oral Presentation, CIBERER (Rare Diseases Network in Spain), Barcelona, 12-14 March 2018
- Redox-dependent Mitochondrial dynamics impairment in adrenoleukodystrophy. Oral Presentation by Dr N Launay, CIBERER (Rare Diseases Network in Spain), Barcelona, 12-14 March 2018
- Aberrant regulation of the GSK-3β/NRF2 axis unveils a novel therapy for adrenoleukodystrophy, Poster presentation at ESHG, Milan 15-19th June
- Precision medicine for the Leukodystrophies: novel genes, mechanisms and therapies. Grand Rounds Speaker of the Medical Genetics Department. Mayo Clinic, Rochester Minnesota, USA. August 8th 2018
- Precision medicine for the Leukodystrophies: from diagnostics to therapy in one go. Invited Speaker. 4th International Symposium on Multiple Sclerosis and Myelin Disorders. Berlin, Germany, October 12th-14th 2018

Relevant scientific publications (selected and / or published by the center)

- Aberrant regulation of the GSK-3β/NRF2 axis unveils a novel therapy for X-ALD.Ranea-Robles P, et al. EMBO Mol Med. 2018 Aug;10(8). pii: e8604. doi: 10.15252/emmm.201708604.
- Epigenomic signature of X-ALD predicts compromised oligodendrocyte differentiation. Schlüter A, et al. Brain Pathol, 2018 Feb 24.
- Allelic Expression Imbalance Promoting a Mutant PEX6 Allele Causes Zellweger Disorder. Falkenberg KD, et al Am J of Hum Genet, 2017;101(6):965-976.
- Oxidative Stress and Mitochondrial Malfunction are interlinked in PM Disease.Ruiz M, et al. Brain Pathology, 2017:5
- De novo mutations in protein kinase genes CAMK2A and CAMK2B cause intellectual disability. Küry S, et al. Am J of Hum Genet, 2017;101(5):768-788.
- Mutations in BRPF1 Cause an Autosomal-Dominant Form of Intellectual Disability with Associated Ptosis.Mattioli F et al. Am J Hum Genet. 2017 Jan 5;100(1):105-116.
- Uniparental disomy unmasks recessive mutations of FA2H/SPG35 in 4 families. Soehn AS, et al. Neurology. 2016;87(2):186-91

Grants. a) grant award to announce funding for projects; b) Received grants from other organizations/institutions for undiagnosed rare diseases research.

1. Precision Medicine for Adrenoleukodystrophy: Identification of Predictive Biomarkers and Neuroinflammation Pathomechanisms. Spanish Institute for Health Carlos III. FIS PI17/00916; 282.000 € (2018-2020).
2. The Undiagnosed Rare Disease Program of Catalonia (URDCat). Personalized Medicine based on Genomics for Undiagnosed Neurological Diseases. Coordinator: Luis Pérez-Jurado. PI: A. Pujol (16 PIs), 1.2 M € total, (2017-2020) 89.000 € for our group.
3. Efficacy of pioglitazone administered to patients with adrenomyeloneuropathy: a phase II, single-arm,multicentric trial.Spanish Institute for Health Carlos III. ICI14/00076; 157.300 € (2015-2018).
4. Systems Biomedicine for identification of novel genes and modeling cortical motorneuron disease. Marato de TV3. 398.000 € (2015-2018)

Contact person

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