and COL1A1 mRNA levels were increased in the dermal fibroblasts of SSc patients suggesting the important role of NLRP3 inflammasome activation in the pathogenesis of SSc.

P-08.5-08
Generation and phenotypic characterization of a transgenic mouse model for a neurodevelopmental rare genetic disorder

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During a whole exome sequence (WES) screen aiming to identify novel candidate genetic mutations that cause neurodevelopmental disorders in pediatric patients, we detected an 11 bp deletion mutation in the ATG9B gene. The patients, children of a consanguineous marriage, displayed mental retardation, facial dysmorphia, obesity, and behavioral abnormalities. The deletion mutation resulted in frameshift and addition of a premature STOP codon, truncating the ATG9B protein. This is a novel autosomal recessive genetic disorder, also the first genetic disease linked with ATG9B. ATG9B is a homolog of ATG9A, a ubiquitously expressed autophagy mediator that acts as intracellular membrane carrier towards phagophore assembly sites. There is plenty of literature on ATG9A and its roles in autophagy. However, ATG9B, whose expression is restricted to placenta and pituitary gland, has not been investigated. We hypothesized; the clinical anomalies observed in patients resulted from abnormal placental development due to ATG9B truncation. When expressed in mammalian cells, the mutant ATG9B aggregates and sequesters in a perinuclear compartment while WT protein displays a distribution similar to ATG9A and localizes as perinuclear and cytosolic puncta. We generated ATG9B knockin mice by inserting a STOP codon at the mutation site, and constitutive ATG9B KO mice by exon deletion. Homozygous knockin and knockout mice were viable. Currently, we are phenotyping the mouse models by analyzing the development, autophagy and apoptosis in placental histological sections. Behavioral tests are in progress. In summary, we identified a novel rare genetic disease, generated transgenic knockin and knockout mouse models, and we expect to accumulate additional data on the disease etiology and ATG9B's functions during placental development by FEBS 2023. This project is completely novel, aims to present a novel genetic disease with in depth characterization, ready to start strategizing potential remedies.

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Abstract withdrawn.

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Dissecting the role of lipocalin in *Plasmodium falciparum* malaria

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Malaria, caused by Plasmodium parasites, is an infectious disease responsible for millions of cases and deaths yearly. Despite the efforts, the disease control has been continuedly threatened by the resilient capacity of the parasite to acquire resistance to antimalarial drugs treatment, which target the symptomatic intraerythrocytic developmental cycle. During this cycle, *Plasmodium falciparum* uptakes hemoglobin from the host cell as a source of nutrients and to free space for growth. Hemoglobin digestion happens in the parasite's acidic food vacuole, where the resultant heme pool is detoxified through biomineralization into hemozoin. However, the mechanism of hemozoin synthesis is still unresolved. The area is highly controversial, with various compounds proposed to catalyze hemozoin formation. Theories include membrane lipids, histidine-rich proteins, the heme detoxification protein and, recently, the transport protein lipocalin, involved in the motion and morphology of the hemozoin crystals. Taking advantage of the advances in gene-editing and functional studies, we targeted the *P. falciparum* lipocalin, aiming to identify its role in hemozoin synthesis pathway, as well as its interactome. This work contributes to a better understanding of the underlying process that being vital and unique by the parasite is the prime target of most present antimalarial drugs. Furthermore, it uncovers novel players into this pathway, which remains a suitable target for next-generation antimalarial drugs. This work was supported by NORTE-01-0145-FEDER-028178 funded by NORTE 2020 Portugal Regional Operational Program under PORTUGAL 2020 Partnership Agreement through the European Regional Development Fund and the by Fundação para a Ciência e Tecnologia (FCT). V Baptista thanks FCT for the SFRH/BD/145427/2019 grant. MI Veiga and S Catarino thank FCT for their contract funding provided through 2020.03113.CEECIND and 2020.00215.CEECIND, respectively.

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Relevance of dipeptidyl peptidase 4 in SARS-CoV-2 infection in patients with type 2 diabetes mellitus

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Type 2 diabetes mellitus (T2DM) is a risk factor for severity and mortality in patients with COVID-19. In addition, a high prevalence of obesity has been observed among patients admitted to intensive care for SARS-CoV-2. Among the new treatments for T2DM,

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