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# G4, A NEW TRANSGENIC MOUSE MODEL FOR POLYCYSTIC OVARIES SYNDROME

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Polycystic ovary syndrome (PCOS) is the number one cause of female infertility. Some mouse models are available to study it. These models are generated by different methods (mainly via administration of dihydrotestosterone) because its origin is not fully understood. A genetic cause has not been confirmed yet. Via insertional mutagenesis, we identified a new gene (*Gm10800*), which when disrupted in mice appears to phenocopy human PCOS. We are currently characterizing this transgenic mouse model (G4), have validated it as a PCOS model, studying the link between *Gm10800* and the observed phenotypes (obesity and sub-fertility). The main features of this model are: 1. Obesity with associated abnormalities such as glucose and insulin intolerance, polyphagia, high leptin levels, and lipid deposition in the ovaries. 2. Sub-fertility associated with cysts in the ovaries, di-estrous arrest, high percentage of non-viable oocytes, and high levels of LH, estrogen and testosterone. The gene disrupted by transgenic insertion (*Gm10800*) appears to be the mouse ortholog of a human gene known as PIRO *(progranulin-induced receptor-like gene during osteoclastogenesis)*. There is a single paper that discusses this gene, suggesting a role for it in the formation of osteoclasts. In accordance with this, our preliminary micro-CT analyses of bone mass density show that transgenic mice have greater bone mass than controls. Ongoing work is aimed at determining how *Gm10800/PIRO* contributes to the observed phenotypes. In conclusion, the G4 mouse model points to a direct link between PCOS and a gene for the first time. It's also the most representative model of PCOS currently available. This makes it an extremely valuable model to better understand the disease and the mechanism of action of some existing medication for it like metformin. It also gives us a precious chance to test new drugs on this model like endoplasmic reticulum stress inhibitors that are already in the drug market for other diseases, like TUDCA (Tauroursodeoxycholic acid).

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