The Wilms' tumor suppressor gene is expressed in adult cardiomyocytes and it regulates myocardial metabolism and response to damage

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The Wilms tumor suppressor gene (*Wt1*) encodes a C2H2-type zinc-finger transcription factor that participates in transcriptional regulation, RNA metabolism and protein-protein interactions. WT1 is critically involved in the development of several organs, including kidneys and gonads, spleen, adrenals, liver, and diaphragm (Hastie, 2017). WT1 is highly expressed in the embryonic epicardium where it regulates a process of epicardial-mesenchymal transformation and the development of the epicardial-derived cells.

We have recently shown evidence of a transient Wt1 expression in about 25% of cardiomyocytes of mouse embryos. Conditional deletion of this expression in the cardiac troponin T lineage caused abnormal sinus venosus and atrium development, thin ventricular myocardium and, in some cases, interventricular septum and cardiac wall defects (Díaz del Moral et al., Front Cell Dev Biol. 2021;9:683861).

We aimed to know if Wt1 is also expressed in adult cardiomyocytes and what could be the consequences of its conditional deletion for cardiac homeostasis and/or in the response to damage induced by isoproterenol and doxorubicin treatments. For conditional deletion of Wt1 in cardiomyocytes, we generated tamoxifen inducible Wt1 mutants by crossing αMHC^{MerCreMer} mice with homozygous Wt1 conditional mice, where the first exon of *Wt1* is flanked by loxP sites.

We have found experimental evidence of a low expression of Wt1 in postnatal murine cardiomyocytes, using reporter and lineage tracing models as well as qPCR. Our preliminary data suggest that conditional deletion of Wt1 in cardiomyocytes induces interstitial fibrosis, increased oxidative stress markers, altered metabolism and mitochondrial dysfunction in Wt1-deficient cardiomyocytes. In addition, conditional deletion of Wt1 in adult cardiomyocytes increases the damage induced by doxorubicin and isoproterenol treatments. These findings suggest a novel role of Wt1 in myocardial physiology and protection against damage.