**Congenital heart disease (CHD)** is the leading cause of fetal heart abnormalities affecting approximately 8 out of every 1000 newborns (2). CHD has been linked to a variety of causative factors including inheritance, etiology, and the environment of the embryo (maternal environment). The NKX2-5 gene was one of the first genes to be linked to CHD. NKX2-5 is a key regulator of early heart formation in vertebrates, encoding a homeobox transcription factor that interacts with downstream cardiac developmental factors. Most research studies to date have investigated the relationship between CHD and the NKX2-5 gene through etiological and genetic causes (3). While both such causes of CHD account for the majority of all CHD, environmental causes of CHD have recently been shown to be increasing and diversifying, accounting for approximately 2% of all CHD cases. Examples of emerging environmental risk factors of CHD in offspring include anti-retroviral medications, obesity, and diabetes in pregnant female (4). *Despite the association of these emerging environmental risk factors to CHD, little is known how such environmental factors can be inherited to influence the genes such as NKX2-5 governing the proper formation of the heart.*

My **primary goal** is to elucidate the influence of obesity in pregnant females on the NKX2-5 gene and its downstream cardiac developmental factors such as GATA4 and TBX5, and how such changes can result in CHD in progeny. My **hypothesis** is that obesity in pregnant females results in deleterious changes to the NKX2-5 gene and/or interactions between NKX2-5 and key downstream cardiac factors. These changes are then passed down to progeny and give rise to CHD.

**Aim 1: Determine the possible genetic influence of obesity on NKX2-5, GATA4 and TBX5.**

**Approach:** Genetically modified obese mice (ob/ob) will be used in this experiment. Following a specific stage of obesity, ob/ob female mice will be crossed with wt male mice. After giving birth, the ob/ob females and their progeny will be sacrificed. The heart of the progeny and the ob/ob females will be sequenced using next generation sequencing.

**Rationale:** By sequencing the genome of mice heart ob/ob mothers and their progeny, we can identify possible genetic mutations that may occur to the NKX2-5, GATA4, and/or TBX5 regions by comparing their DNA sequences to each other and to the reference genome of wildtype mice.

**Hypothesis:** Conserved mutations across mouse progeny and the ob/ob mothers will be apparent in at least one of the cardiac genes of interest.

**References**

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