

## Master Internship - Biomedical Science

<p><b>Title Project</b> Assessing the difference in differentiation capacity between mesenchymal stromal cells derived from the umbilical cord of mono chorionic twins to chart functional consequences of an adverse prenatal environment</p>
<p><b>Department and research group</b> Leiden University Medical Center Molecular Epidemiology, Department of Biomedical Data Sciences</p>
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<p><b>When is project available?</b> Starting April/ May for 6 month or longer (fulltime)</p>
<p><b>Background and Research Questions</b> Lifelong health is thought to be partially set during intrauterine life by persistent epigenetic changes induced by the prenatal environment. To evaluate this hypothesis, we initiated a prospective longitudinal study in mono chorionic (MC) twins that started in January 2019: The Twinlife study <sup>1,3</sup>. MC twins are monozygotic, thus in origin genetically identical, and share a single placenta. Although MC twins have many environmental factors in common, in one-third of the MC twin pairs one fetus has significantly less access to nutrients and resources during pregnancy than its co-twin, often resulting in a significant discordance in prenatal growth and birth weight. Hence, MC twins constitute a unique natural experiment to study the influence of the prenatal environment on health. In the Twinlife project, we use mesenchymal stromal cells isolated from umbilical cord (hUC-MSC) as an advanced proxy to gain more insight in the mechanism behind the effects of epigenetic dysregulation on long-term health consequences. Charting the functional consequences of the adverse prenatal environment on hUC-MSCs is one central aspect within the Twinlife study. Previously, it has been demonstrated that an adverse environment in the womb can influence the differentiation capacity of MSCs. Children born to obese mothers exhibit a greater capacity to differentiate into adipocytes compared to children born to normal weight mothers <sup>2</sup>. We hypothesize that the difference in prenatal nutrient access between the twins also has an effect on the differentiation capacity of the MSCs. To compare the differentiation capacity of MSCs within a twin-pair, there is a need for state-of-the-art differentiation and quantification protocols. During this internship you will focus on setting-up these protocols, characterize and differentiate MSCs derived from different donors and sources, assess differentiation related gene expression by RT-qPCR and compare the differentiation capacity of twins discordant in birthweight as a result of an unequally shared placenta. When MSC differentiation into the diverse lineages is successful, functional differences of the generated cells can be assessed. With this we hope to gain more insights in the mechanistic background of how an adverse prenatal environment is capable to influencing disease risk later in life.</p>
<p><b>Data types, data analysis methods, if applicable, wet-lab techniques</b></p> <ul style="list-style-type: none"> <li>• hUC-MSC culture and characterization (cell culture, Immunophenotyping by FACS, Differentiation)</li> <li>• Aiding the set-up and standardization of differentiation and quantification protocols for hUC-MSCs into different cell types (adipocytes, osteoblasts, chondrocytes, neuronal cells etc.)</li> <li>• Performing literature research on the latest developments in differentiation and quantification protocols</li> <li>• Analysis of differentiation capacity between different conditions as MSCs source variation and intra-twin differences</li> <li>• Expression analysis of differentiation related genes (RNA Isolation, cDNA synthesis, RT-qPCR)</li> </ul>
<p><b>References and further reading</b> <sup>1</sup> Groene, Sophie G., et al. "TwinLIFE: the twin longitudinal investigation of Fetal discordance." <i>Twin Research and Human Genetics</i> 22.6 (2019): 617-622. <sup>2</sup> Boyle, Kristen E., et al. "Mesenchymal stem cells from infants born to obese mothers exhibit greater potential for adipogenesis: the Healthy Start BabyBUMP Project." <i>Diabetes</i> 65.3 (2016): 647-659. <sup>3</sup> <a href="https://en.twinlifestudy.info/">https://en.twinlifestudy.info/</a></p>