‘Uncovering the role of E-cadherin in hematopoietic progenitors to improve anemia in hematopoietic malignancies’

Background

Our research aims to identify treatable causes of anemia by improving our insights into the regulation of red blood cell formation. Anemia is a hallmark of hematopoietic malignancies like myeloid dysplasia syndrome (MDS). MDS reflects a heterogeneous group of hematopoietic neoplasms in the bone marrow, diagnosed in ~500 patients a year in the Netherlands, that harbors the potential to develop into acute myeloid leukemia (AML). Nevertheless the primary cause of death of MDS patients is caused due impaired treatment responses to the developed anemia. Therefore improved insights into anemia development are needed to develop novel treatment options and improve clinical outcome.

Recently we uncovered E-cadherin to critically control the production of Red Blood Cells in health human bone marrow derived hematopoietic progenitors. Whereas E-cadherin is well established to act as a master regulator of cell junction integrity in epithelia and to act as an important tumor suppressor, little is known about the role of E-cadherin in Red Blood Cell production. Importantly, increased E-cadherin expression marks erythroid malignancies, characterized by life-threatening anaemia, such as pure erythroid leukemia (PEL) and MDS. This internship will explore the molecular pathway down stream of E-cadherin which controls the production of Red Blood Cell formation in healthy and malignant human hematopoietic progenitors.

Research Questions

- What is the underlying mechanism by which E-cadherin controls the production of Red Blood Cells?
- Does manipulation of E-cadherin signaling enhance red blood cell formation in MDS?

Approach

During this internship you will isolate hematopoietic progenitors (HPCs) form healthy and MDS-derived bone marrow to assess cell growth and differentiation of these HPCs in an vitro culture system which is optimized to drive the formation of red blood cells. You will employ state-of-the art molecular techniques to manipulate E-cadherin signaling in these cells such as knockdown strategies as performed by shRNA and Crispr-Cas9. The obtained results will be used to assess the feasibility to improve anemia in MDS patients and hence performed in close collaboration with the research group of prof. Arjan van de Loosdrecht at the VUmc/UMC.

Your profile

A highly-motivated master student in medical science looking for a master internship in an innovative and exciting field of hematology.

Additional Information

Head research group: Dr. M.Nethe (m.nethe@sanquin.nl)
Start date: Direct
Duration: 9 months