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Junior Clinician Scientist
nTTP-GCT-Jahrgang 2025

Klinik für Pädiatrie m. S. Pneumologie, Immunologie und Intensivmedizin
CHARITÉ - UNIVERSITÄTSMEDIZIN BERLIN

Forschungsbereiche:

- Immunodeficiencies Affecting T Cellular Immunity
- Thymic Stromal Cell Development and Function
- Pediatric Immunology

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Translational Scientist
nTTP-GCT-Jahrgang 2025

BERLIN INSTITUTE OF HEALTH IN DER CHARITÉ (BIH)

Forschungsbereiche:

- iPSC Differentiation
- T Cells, Regulatory T Cells
- Epigenetics
- (Epi-) Genome Engineering

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Combining novel *in vitro* T cell differentiation systems for improved SCID diagnosis and for T cell product generation

Projektbeschreibung:

In vitro systems to model human T cell development can be used to assess the T cell differentiation potential of hematopoietic precursor populations, enabling diagnosis and research of diseases with impaired T cell development such as genetically undefined severe combined immune deficiency (SCID), a fatal disease if left untreated. In addition, *in vitro* differentiation systems can be used for generation of human T cell populations – an approach which holds great promise for adoptive cell therapeutic approaches to treat various diseases including cancer and autoimmunity.

In the present project, junior clinician scientist (JCS) Dr. Sarah Dinges and the translational scientist (TS) Dr. Christopher Kressler join forces and combine their complementary expertise on *in vitro* models of T cell differentiation. Sarah Dinges worked previously with the Artificial Thymic Organoid (ATO) system. The system can correctly identify different forms of SCID, but is technically challenging, time-consuming (8 weeks) and requires a feeder cell line. Christopher Kressler established a feeder free T cell differentiation system, which relies purely on defined media and stimulation components. It has been successfully used to generate double positive T cells. Still, it doesn´t allow the differentiation of CD4 single positive T cells, needed for regulatory T cell (Treg) cell based therapies.

We will establish the Artificial Thymic Organoids (ATOs) system as a test for the diagnosis and treatment decisions for SCID patients in Germany (work package1, WP1). Next, we will transfer SCID diagnosis to the feeder free system, making it more robust and less labor intensive (WP2). Finally, in WP3+4 we want to demonstrate proof-of-concept (PoC) CD4 T cell and Treg product generation from induced pluripotent stem cells (iPSCs). This would pave the way for an off-the-shelf solution, omitting the currently required patient specific generation of cell products (WP3+4).

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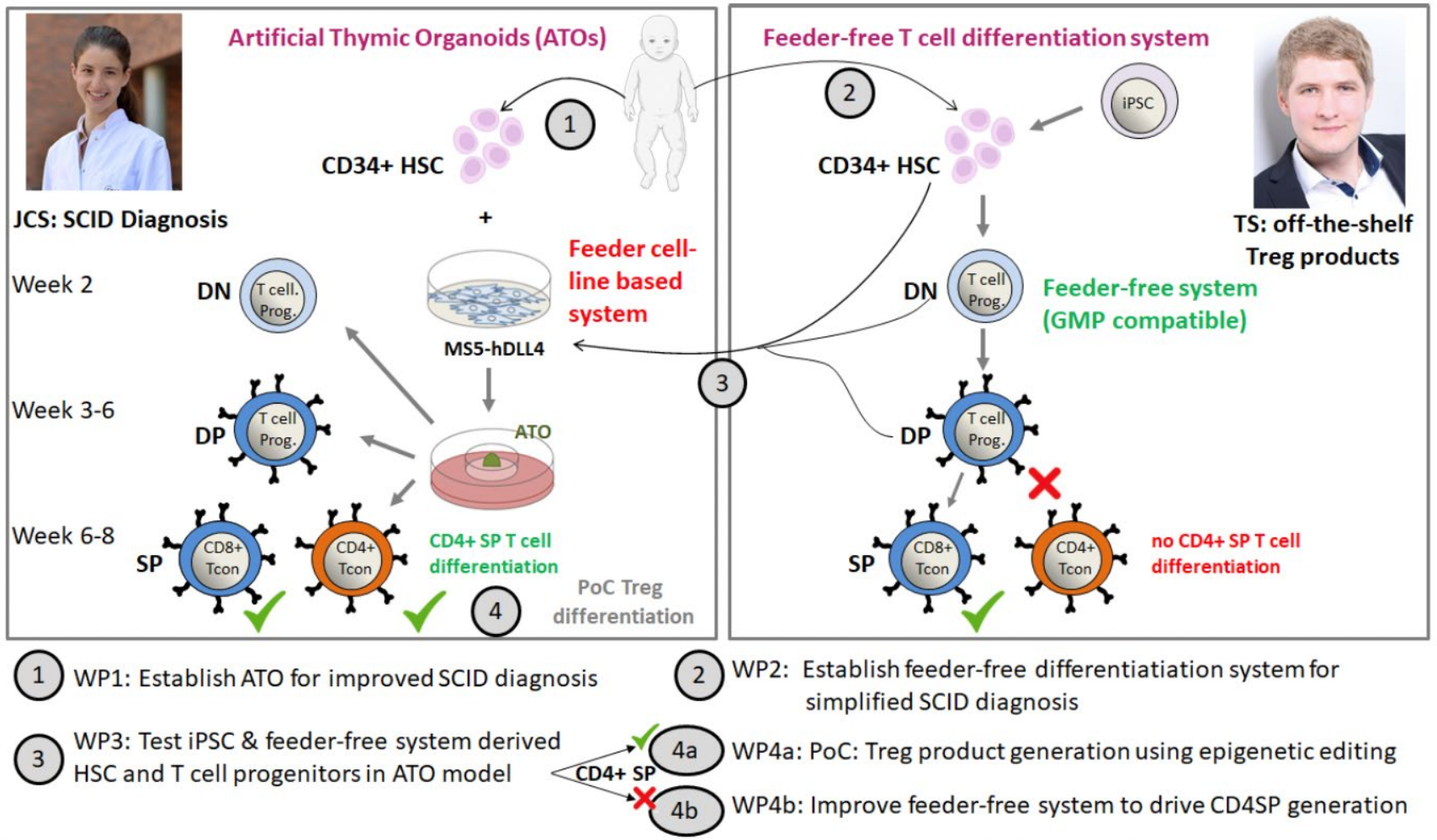

Figure 1: Visual project summary. The two in vitro T cell differentiation systems and their use within work packages (numbers) during the nTTP-GCT projects are displayed.