Curriculum ITCC Fellow at University Children´s hospital Muenster

Clinical experience:

The basic training will be provided by active participation and training within our Early Clinical Trials Unit, with both in- and outpatient beds on our two wards and a clinical trial office staffed with 6 study nurses/data managers and a secretary. Our team of PIs are the attending physicians and head of our Department, all highly experienced in the preparation and performance of clinical trials and with specific backgrounds and expertises in all three areas of haematological, solid and CNS cancers (Leukemia: C. Rössig, Lymphoma: B. Burkhardt, Sarcoma: B. Fröhlich, Neurooncology: K. Kerl, HLH/LCH: M. Ahlmann), including the allogeneic stem cell transplant setting and cell therapies, with a specific focus on CAR T cell trials (Rössig). The fellow will further gain experience in supportive care phase I/II clinical trials e.g. for infectious complications (PI A. Groll).

We have 4 tumor boards, each held weekly:
- "Ped Onc Radiology board": Diagnostic imaging and response assessment by a highly experienced Pediatric Radiologist.
- "Bone tumor board": Diagnosis (imaging + pathology demonstration) and interdisciplinary management of CAYA patients with bone tumors (Ped Onc, Med Onc, Radiology, Orthopedic Surgery, Thoracic Surgery, Radiotherapy, Pathology)
- "Neurooncology board": Diagnosis and management of patients with CNS tumors (Ped Onc, Med Onc, Neuroradiology, Neurosurgery, Neurology)
- "Ped Onc Tumor board": Interdisciplinary management of pediatric patients with hematological and solid cancers (Ped Onc, Ped Radiology, Radiotherapy, Orthopedic Surgery, Thoracic Surgery, Pediatric Surgery, further surgical disciplines)

Closely supervised by the PI, the fellow will be continuously and directly involved in the management of children and adolescents treated on phase I/II trials, including patient selection, information and consenting of patients and their families, patient screening and eligibility.
Together with our data managers and the PI, the fellow will organize and attend patient visits, keep notes and keep CRFs. She/he will be trained by the PI in recognizing and CTC grading of general and drug-specific toxicities and in the clinical management. She/he will record (S)AEs and SUSARs and be involved in the reporting. She/he will be trained and actively involved in the coordination of patient sample collection and transfer (PK, PD, PG, biology). She/he will participate in the SIVs, in trial TCs, trial monitoring visits, close out visits, audits and regulatory inspections, and in our weekly internal Investigator Meetings. The fellow will participate in our regular tumor boards outlined above where she/he will be involved in the radiological response assessments, including immunological response criteria, and into the multidisciplinary cooperation and communication which lies the basis for effective innovative cancer therapy. She/he will further participate in the molecular tumor boards (INFORM, ILTB, FEDRALL, and occasionally STEP and others), followed by internal discussions and patient-individual decisions in the Ped Onc Tumor Boards.
Our center further provides the opportunity to gain experience in the adult clinical trials unit (Director: Prof. Dr. Georg Lenz), also covering both haematological and solid cancers.

In parallel to the basic training, after an initial 4-weeks training period exclusively spent in the early phase unit of the Department, we will provide the fellow with a structured curriculum of 13 rotations (35 weeks) rotations into various labs and related disciplines. To allow for an uninterrupted basic training and continuous involvement into the management of the patients, these will be half-day rotations, usually in the afternoons, along with full days when the patient visit schedule allows it (at least 1 full day per week of rotation). In detail, the following rotations will be organized:

Preclinical drug development

Insights will be provided by three 2-week rotations into selected **research laboratories in** our Department. The fellow will chose from the following labs:

Prof. Rössig: Topics: Immuno-Oncology, immune targets, microenvironment, CAR T cells; Technologies: Immune function assays, lenti-/retroviral gene transfer, T cell/NK cell culture, multicolor immunohistochemistry, multiparameter flow cytometry
Prof. Burkhardt: Topics: Lymphoma biology, biomarker discovery, key pathways
Technologies: NGS, including big data analysis, target identification/validation
Prof. Kerl: Topics: Tumorigenesis of rhabdoid tumors/embryonal brain tumors, epigenetics
Technologies: Single cell transcriptomics, genetically modified mouse models
Dr. Balbach: Topics: Epigenetic signatures of sarcomas and leukemias
Technologies: CRISPR/Cas9 screening, target analysis
In addition, the fellow will be invited to participate in the weekly journal club meetings and progress reports of the Experimental Research Program of the Department, and in the annual retreat. Moreover, she/he is invited to join the teaching events (lecture series, brown bag lunch) of the cluster of excellence "CiM" (Cells in Motion, https://www.uni-muenster.de/Cells-in-Motion/index.html).

The fellow will further rotate into the **Pharmaceutical Chemistry Department** (Contact: Prof. Hempel) for 2 weeks to study all aspects of pharmacokinetics, including standard PK parameters as well as modeling and population PK. Specific issues with the small sample sizes available from pediatric patients will be addressed.

Protocol development and regulatory issues will be taught in an 8-week rotation into the local clinical trial center, **ZKS Münster** (https://www.medizin.uni-muenster.de/zentrum-fuer-klinische-studien-muenster/das-zks.html) and a 4-week rotation into the **NHL study group** (Prof. Burkhardt) (https://www.ukm.de/index.php?id=7452). Specific biometric aspects of pediatric trials will be studied within a 2-week rotation into the **Institute of Biometrics and Clinical Studies** (Prof. Faldum).

To supplement the training with respect to Hematology trials, the fellow will rotate for 1 week into the interdiscipinary (pediatric + adult) **Cytomorphology lab** of our Department and be actively involved into the cytomorphological and flow cytometry response assessments.The fellow will further rotate into the **Department of Pathology** (Prof. Hartmann) (2 weeks) where she/he will understand histological (IHC, e.g. PD-L1) and genetic (NGS panel) marker analysis.

For training in aspects of pharmaceutical industry, we will approach our contact persons, usually the Medical Monitors, of the **pharmaceutical sponsors** of our ongoing non-ITCC trials (e.g. Pfizer, Novartis, Miltenyi Biomedicine). Miltenyi in Bergisch Gladbach has already offered to accept fellows within this program for 2-week rotations.

Palliative care and ethical aspects are a fundamental component of the clinical management of pediatric and adolescent patients in early phase clinical trials in which the fellow will be actively and regularly involved.

In addition, two rotations within the accompanying curriculum will focus on these aspects:

Palliative care team of our Department, Contact Dr. M. Baumann-Köhler (https://www.ukm.de/index.php?id=4330):
4-week half-day rotation, including patient visits in the hospital and at their homes, participations in team conferences and decision-making.

Ethics committee of the Westfalian Wilhelms University and Ärztekammer Westfalen-Lippe, Contact Prof. Wolfgang Berdel (https://www.medizin.uni-muenster.de/ethikkommission/ethik-kommission/)
2-week half-day rotation, including participation in at least 3 committee meetings. In addition, the fellow will join the PId in presentations of trials in Ethical Board committee meetings throughout the fellowship.