LS25-044 - Predicting the evolution of relapse in Wilms tumour using drug sensitivity profiling and liquid biopsies

Zusammenfassung

Children with relapsing Wilms tumours have a dramatically reduced survival rate, yet predicting which patients will recur remains challenging, with over half of relapsing patients not being flagged as high-risk. To address this, we will combine minimally invasive liquid biopsy genomic profiling and high-throughput drug screening to estimate when patients will recur using evolutionary modelling. Our aim is to test the feasibility of a prognostic assay that could be rapidly implemented clinically (with minimal intervention) across Wilms tumour patients in Europe to guide patient-specific prediction of relapse.

To achieve this objective, we will build on our expertise in liquid biopsies, paediatric tumour genomics and evolutionary modelling. We will sequence circulating tumour DNA in liquid biopsy samples from 50 Wilms tumour patients (25 relapsing) retrospectively from diagnosis, initial chemotherapy, surgery and follow-up using shallow whole genome sequencing (copy number alterations) and targeted sequencing (driver mutations). In a relapsing subset we will also assay additional follow-ups and relapse (Aim 1). We will combine our assessment of clonal dynamics with drug screening of cell models with high-risk mutations (Aim 2) and utilise our findings to understand mutation-specific responses to common therapies and novel agents. We will then predict patient relapse in a real-time setting using modelling and we will perform this prospectively in ~10 patients in Austria and Germany (Aim 3). Our goal is to enable clinicians to adapt treatment according to patient-tailored genetic (liquid biopsy) and phenotypic (drug sensitivity) readouts in future.

Centring our efforts on Wilms tumour, an entity with high inter- and intra-tumour heterogeneity, we will test the predictability of patient outcomes using cutting-edge methods in precision oncology. Our multidisciplinary, international team, with long-standing clinical links, will ensure rapid translation of our findings.

Wissenschaftliche Disziplinen:
Cancer research (40%) | Genomics (30%) | Cell biology (30%)

Keywords:
Paediatric cancerWilms tumourCancer genomicsDrug screeningLiquid biopsiesCancer evolution

---

Principal Investigator:	George Cresswell
Institution:	St. Anna Kinderkrebsforschung GmbH (CCRI)
Co-Principal Investigator(s):	Sabine Taschner-Mandl (St. Anna Kinderkrebsforschung GmbH (CCRI)) Jenny Wegert (Uniklinikum Würzburg)

Status: Vertrag in Vorbereitung
GrantID: 10.47379/LS25044

Weiterführende Links zu den beteiligten Personen und zum Projekt finden Sie unter
https://wwtf.at/funding/programmes/ls/LS25-044/