The DKTK EXLIQUID consortium – Exploiting liquid biopsies for molecular tumor board patients

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Background & objectives

Testing for genetic alterations in tumor tissue has become an essential tool in clinical practice for personalized cancer therapy. EXLIQUID is a liquid biopsy consortium established in 2021 within the DKTK (German Consortium for translational cancer research). It comprises members of 12 university hospitals in Germany. With this consortium, we are addressing the urgent clinical need to assess liquid biopsies (LBs) for therapy selection and monitoring for patients seen in molecular tumor board (MTB).

Methods

So far, we have established a multicenter repository of high-quality LB samples with the focus on rare solid cancers. We are collecting blood samples from MTB patients at first registry at the MTB, at the beginning of the treatment, and at each subsequent patient visit until recurrence. Samples from selected cohorts are finally subjected to comprehensive profiling with the focus on cell-free DNA (cfDNA).

Results

Within the consortium we have defined projects that focus on cfDNA-based kinetics of tumor mutant variants. Within these, we evaluate their value to predict early treatment failure, to assess the median lead time between molecular and clinical progression, and to shed light on clonal evolution dynamics associated with therapy resistance. In further projects, we explore the potential of epigenomic alterations in cfDNA. Aberrant DNA methylation is a hallmark of cancer, and many hyper- or hypomethylated genomic sites can be used to monitor molecular tumor dynamics irrespective of DNA mutation status for early prediction of therapy resistance. In addition, epigenetic analysis could also inform about tissue of origin in patients with cancer of unknown primary.

Conclusion

By bringing together experts from all DKTK partner sites with their complementary local expertise, skills, and established technologies, we hope to be able to overcome existing challenges in the translation of liquid biopsy into clinical routine. Due to its large-scale multicenter setup, the EXLIQUID consortium can help to identify liquid biomarkers in less common tumor histologies and genotypes, which will enlarge the scope of patients who will benefit from LB in the future. Besides this scientific relevance, EXLIQUID is building a

valuable precision oncology cohort which will be available for future collaborative research studies within the DKTK network and beyond.