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Promotionsverfahren von **Frau M.Sc. Stella Maris Pauls**
Auslage der Dissertation und Gutachten sowie Termin der mündlichen Prüfung
Anlage: Einseitige Zusammenfassung der Dissertation

Sehr geehrte Damen und Herren,

in dem oben genannten Promotionsverfahren wird die Annahme der Dissertation

Characterization of proteomic signature of pancreatic and testicular carcinomas by new sensitive methods for scarce FFPE tissue proteomics

von den Berichterstattenden Prof. Dr. K. Stühler und Prof. Dr. A. Reichert beantragt. Sie kann zusammen mit den Gutachten in der Zeit

vom 04.01.2025 bis 15.01.2025

eingesehen werden. Bitte wenden Sie sich zur Einsicht an das Promotionsbüro (promotionmnf@hhu.de).

Einsprüche gegen diese Dissertation können nur zwei Tage nach der vorgenannten Frist geltend gemacht werden. Erfolgt kein Einspruch, so gilt die Dissertation als angenommen (§ 7 Ziffer (5) PO).

Sofern die Dissertation angenommen wird, findet die mündliche Prüfung am

20.01.2025 um 13:00 Uhr

im **Raum 22.07.U1.025** statt. Als Prüferinnen bzw. Prüfer sind vorgesehen:
Prof. Dr. G. Klau, Prof. Dr. Eva Nowack und Prof. Dr. G. Groth.

Die Öffentlichkeit ist bei der Befragung zugelassen.

Mit freundlichen Grüßen
im Auftrag

Silke Krispin

Summary

Stella Maris Pauls

FFPE tissues are an important source for gaining new insights into various diseases mechanisms. Many helpful methods, such as laser microdissection, can aid in examining biological processes at the cellular level from the fixed tissue material. With new, sensitive sample preparation and data acquisition methods, it is possible to enable deep proteome analyses to advance the study of various proteins involved in disease mechanisms. This work primarily focuses on cancer research regarding pancreatobiliary and testicular cancers. The optimized sample preparation for LC-MS/MS based proteomics allows for the discovery of new drug targets, biomarker candidates, and give biological insights into disease development. In the field of testicular carcinomas, new insights into drug resistance of recurring yolk-sac tumors have been gained. These findings help develop new antibody-drug-conjugates to treat these resistant tumors and enable broad drug screenings. Furthermore, the biological processes involved in the development of therapy resistance were explored using multiomic applications (genomics, methylomics, proteomics), revealing the tissue of origin (teratomas) from which germ cell tumors develop. The robustness of the sample preparation methods also makes it possible to study FFPE tissues of very rare diseases using LC-MS/MS-based proteomics. The growing teratoma syndrome (GTS) is a rare subform of germ cell tumors, characterized by a reduced occurrence of tumor markers during chemotherapy treatment and continuing uncontrolled growth. Here, insights into the biological processes involved in the development of GTS are provided, achieved through multiomic approaches (genomics, methylomics, transcriptomics, proteomics, secretomics). Finally, the optimized FFPE sample preparation methods are applied to laser microdissected FFPE tissues of precursor lesions from pancreatic cancer, enabling a new multiomics approach. Using a data-independent acquisition (DIA) method, it was possible to uncover parts of both the entire proteome and the O-glycoproteome in the recorded mass spectrometric dataset. This analysis provided insights into the diverse biological processes underlying the progression of precursor lesions into carcinomas. Additionally, it is shown that the T/Tn antigen glyco-modification and its sialylated subforms are increasingly found on many different proteins in the tumor-developing tissue lesions, supporting the thesis that these modifications accumulate more in tumor tissues. The protein 14-3-3 theta was identified as a potential biomarker candidate in a differential modification analysis, with the Tn antigen and the sialylated form being more prevalent in tumor-developing tissues. The optimized sample preparation methods presented here are suitable for very small amounts of FFPE tissue, as well as for sample sets with highly variable tissue quantities, as they ensure high sensitivity and reproducibility.