
Half time review seminar 2021-03-25

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Background
Pancreatic cancer is a dismal disease with limited therapeutic options. Hence, chemotherapy remains standard of care, with no predictive biomarkers in clinical use. Adding to this, tumour heterogeneity contributes to the emergence of treatment resistance.

Method
My thesis focuses partly on biomarker research based on tumours from a retrospective cohort of 175 patients with resected pancreatic and other periampullary adenocarcinomas, and partly on an ongoing prospective study: Chemotherapy, Host response And Molecular dynamics in Periampullary cancer (CHAMP).

Preliminary results

Paper 1
This study investigated cellular processes and genes regulated by RNA-binding motif protein 3 (RBM3), a promising biomarker of chemotherapy response in pancreatic cancer. Transcriptomes of MIAPaCa2 cells with and without RBM3 knockdown were compared by next generation RNA-sequencing. The top down-regulated gene PDS cohesion associated factor A (PDS5A), the top up-regulated gene cyclin D3 (CCND3) and the top prognostic gene Proline rich 11 (PRR11), all involved in cell cycle and cell division, were selected for further investigation. Immunohistochemical analysis of tumours in the retrospective cohort revealed that high expression of PRR11 was an independent factor of poor prognosis.

Paper 2
This paper is a study protocol of the CHAMP study, a prospective, single-arm observational study that started in 2018. In brief, comprehensive genomic and immune profiling is applied on tumor tissue and repeated on-treatment blood samples to study the spatial and temporal clonal evolution and accompanying host responses in patients with pancreatic/periampullary cancer undergoing adjuvant or palliative chemotherapy treatment.

Paper 3
In this study, we will examine levels of inflammatory cytokines and chemokines during treatment, and how they relate to quality of life-parameters.

Paper 4
TBD.
Significance
The results from the retrospective study further validate the potential clinical relevance of RBM3 as a predictive marker for chemotherapy response in pancreatic cancer, and highlights PRR11 as a novel prognostic biomarker. In the forthcoming studies we hope to gain sufficient knowledge to propose novel strategies for dynamic tumor monitoring and adaptive therapies, with the ultimate goal to improve the quality of life as well as the chances of a prolonged survival in patients afflicted with this devastating disease.

Published paper

Manuscript – to be submitted shortly