ABSTRACTS
- PITCHES RESEARCHERS -

1.Christophe Deben

Accelerate Drug Discovery with DrugVision.AI: High-Throughput Drug Screening on Patient-Derived Tumor Organoids

DrugVision.AI at the University of Antwerp offers an advanced high-throughput drug screening platform utilizing live-cell imaging on patient-derived tumor organoids from the UZA/UAntwerp tumor organoid biobank. Our service enables researchers and pharmaceutical companies to test new compounds in clinically relevant models and identify potential biomarkers and drug potentiators. By leveraging this cutting-edge platform, partners can accelerate their drug development pipeline with data-driven insights directly from patient-derived samples. For more information, visit our website www.drugvision.ai.

2.Winnok De Vos

High-throughput single cell phenotypic profiling reveals selective vulnerabilities in two- and three-dimensional glioblastoma model systems

Glioblastoma is the most lethal primary brain tumor in adults, infamous for its cellular heterogeneity and extensive tissue infiltration. We have established suite of systematic microscopy-based approaches to monitor the state of individual glioblastoma cells in conditions that recapitulate both the physical and multicellular context of their native ecosystem. Informed by complementary proximity proteomics, we have used these imaging tools to expose a mechano-regulatory circuit that drives invasion and which could represent a new targetable vulnerability in glioblastoma disease progression.

3.Senada Koljenovic

Improving oral cancer surgery by intra-operative assessment of resection margins: need for objective techniques

Patients with oral cavity cancer are often treated with surgery. Of the many factors that may affect the clinical outcome of patients with OCSCC (such as tumor site, TNM classification, patient age, comorbidity, and tumor histological characteristics) only the resection margin is under the control of the surgeon and the pathologist. The goal is to remove the tumor with a margin of > 5 mm of surrounding healthy tissue, according to the international guideline of Royal College of Pathologists. This results in the best patient outcome through highest 5-year survival, less need for adjuvant radiotherapy/chemotherapy, better quality of life, less tumour recurrence. This is referred to as “adequate surgery”. However, in the oral cavity region many important and delicate functional tissue structures should be spared if possible. Moreover, it is often impossible for the surgeon to accurately delineate the tumour in the operating room by visual inspection and palpation alone. Unfortunately, as a result only about 15% to 26% of the oral cancer surgeries achieve adequate resection margins.

Intraoperative assessment of tumor resection margins can dramatically improve surgical results. It enables the surgico-pathological team to directly perform additional tissue resection, if necessary, to achieve a so-called “first time right surgery”. However, current methods are laborious, subjective, and logistically demanding. This hinders broad adoption of intraoperative assessment of tumor resection margins, to the detriment of patients. Inadequate resection margins result in the need for a 2nd, sometimes 3rd operation, combined or not with chemotherapy or radiotherapy.

Therefore, an objective easy-to-use technique is needed, to accurately assess all resection margins intraoperatively. The challenges in pathology and the opportunities of photonic techniques in general will be discussed. The development of a high-wavenumber Raman spectroscopic technology, for quick and objective intraoperative measurement of resection margins will be presented.

4.Inge Mertens

Prediction of immune checkpoint inhibitor response in NSCLC

Immune checkpoint therapy with PD-1 and PD-L1 antibodies has revolutionized cancer therapy, with remarkable efficacy in the treatment of several cancers (e.g. melanoma). However, not all patients respond to immunotherapy. For example, evidence is increasingly showing that KRAS mutated cancer cells, that are found in approximately 30% of patients with non-small cell lung cancer (NSCLC) and colorectal cancer (CRC), create an immunosuppressive tumour microenvironment. This demonstrates that **composite biomarkers integrating diverse molecular features will be required to optimally predict treatment responses**. In a preceding study, we performed mass spectrometry imaging (MSI) for peptide analysis on pre-treatment formalin-fixed paraffin embedded (FFPE) NSCLC biopsies, and identified three additional predictive molecules, i.e. human neutrophil peptides (HNP) 1, 2 and 3, also called neutrophil defensins 1, 2 and 3. With the combined presence of PD-L1 expression and the presence of HNP1-3 in the tissue, the false response rate was reduced from 64% (with only PD-L1) to 16%. The shared VITO and University of Antwerp patent for the use of HNPs as predictive biomarkers for anti-PD-(L)1 immunotherapy is pending (EP 19197602.6; G01N33/574, G01N33/68).

In future research, we plan to develop such a composite biomarker to select patients with NSCLC for immune therapy. We will build a **statistic model using already established biomarkers that are measured during routine diagnostic workup of tumour biopsies** (e.g. PD-1/PD-L1 expression, immune cell population measurements, and genomic biomarkers such as tumour mutational burden, gene mutations and copy number variants). We will then aim to **improve the accuracy of this model by adding in newly discovered OMICS markers (e.g. the HNP1-3 peptides), that are not yet routinely assessed**. Besides the HNP1-3 peptides, MALDI imaging will be used on retrospectively collected FFPE tissue biopsies to discover additional predictive peptides. On the same samples, combined bulk and single nuclei RNA-sequencing will be performed to identify expressed tumour (neo-)antigens and HLA subtyping. Finally, we will establish a cohort of prospectively collected fresh frozen tissue samples and plasma samples (including the secreted extracellular vesicles) for validation purposes, and to assess the added value of kinase activity profiling and immunopeptidomics with the highly sensitive TimsTOF SCP. Immunopeptidomics data will also be used to validate the tumour neo-antigens predicted based on bulk/single nuclei RNA-sequencing. Finally, (single nuclei) RNA-sequencing data, untargeted proteomics and O-link technology will provide crucial insights into the pathways and intercellular communication channels that govern immune checkpoint therapy response/resistance in advanced NSCLC patients.
We believe that these immune-related data will help to elucidate the reason why patients do not respond and will uncover new targets for alternative immune related treatments, like cancer vaccines with CAR-T or CAR-NK cells.

5.Eva Lion

The Antwerp ATMP hub: consolidating the cell, gene and tissue engineering ecosystem

6.Severien Van Keer

CASUS: a fully molecular cervical cancer screening approach, based on first-void urine as an easily accessible and non-invasive source of biomarkers

There is a global shift towards implementing self-sampling for cervical cancer screening to reach the WHO elimination targets. This necessitates a triage test after primary HPV testing. DNA methylation analysis provides a promising triage strategy and bypasses the need for an additional visit for a cervical smear due to its compatibility with self-collections, including urine. CASUS aimed to optimize and validate a molecular cervical screening approach based on HPV and human DNA methylation analysis in first-void urine. Hereto, urine samples were collected by 454 females including healthy controls and females diagnosed with cervical neoplasia and cancer. The bi-marker methylation test detected nearly all cancers and a majority of in situ cancers in first-void urine, with similar performance in training and validation cohorts. These data are encouraging and will be further validated in independent (screening) cohorts.

7.Elise Daems

A novel singlet oxygen-based photoelectrochemical platform for the specific detection of nucleic acid-based cancer biomarkers

In recent decades, remarkable scientific and technical advances have occurred in molecular biomarker testing to enable oncologists to specifically diagnose cancers and to accurately match therapies to individual patients. Conventional testing approaches for molecular testing of cancer biomarkers are based on polymerase chain reaction or next-generation sequencing. Despite their high specificity and sensitivity, these established techniques come with significant challenges: high cost (device and consumables), complexity, long time-to-result, and need for trained personnel.

To overcome challenges such challenges, we aim to develop an innovative singlet oxygen ($^1O_2$)-based photoelectrochemical platform for the detection of cancer biomarkers. Our technology combines (i) photosensitisers that produce $^1O_2$ upon illumination, (ii) a redox reporter, and (iii) magnetic beads for immobilisation and enhancing sensitivity. Moreover, the technology is target fast, amplification-free, enzyme-free and eliminates matrix effects because of a light on/off switching mode.
Within this work, we mainly focused on detecting single-point mutations in the KRAS oncogene (Kirsten rat sarcoma virus), which play an important role in e.g. colorectal cancer. Crucial for detecting mutations is distinguishing them from wild-type sequences, which was accomplished via precise temperature control. Additionally, we developed a multiplexing setup to enhance usability that allows (i) a readout of 96 samples within 15 minutes, and (ii) the analysis of multiple biomarkers in one well.

8.Ken Op de Beeck

IMPRESS: improved multiplex methylation profiling using restriction enzymes and smMIP sequencing for highly sensitive multi-cancer detection

<u>Background</u>
Despite the worldwide progress in cancer diagnostics, more sensitive diagnostic biomarkers are needed. The methylome has been extensively investigated in the last decades, but a low-cost, bisulfite-free detection methods for multiplex analysis are still lacking.

<u>Methods</u>
We developed a methylation detection technique called IMPRESS, which combines methylation-sensitive restriction enzymes and single-molecule Molecular Inversion Probes. DNA is digested using four MSREs. As such, methylated CpGs remain intact, while unmethylated CpGs are cleaved.
We validated IMPRESS by designing a multi-cancer detection assay for eight of the most lethal

cancers worldwide. 1,791 CpG sites were validated in 35 whole blood, 111 tumor and 114 normal samples. Finally, a classifier model was built.

Results
We present the successful development of IMPRESS and validated it with ddPCR. The final classifier model discriminating tumor from normal samples was built with 358 CpG target sites and reached a sensitivity of 0.95 and a specificity of 0.91. We show that IMPRESS works with input DNA as low as 5ng and we provide data that highlight IMPRESS's potential for liquid biopsies.

Conclusion
We successfully created an innovative DNA methylation detection technique. By combining this method with a new multi-cancer biomarker panel, we developed a sensitive and specific multi-cancer assay, with potential use in liquid biopsies.