The Development of Antibodies and Characterisation of Novel Prognostic Biomarkers in Colorectal Cancer

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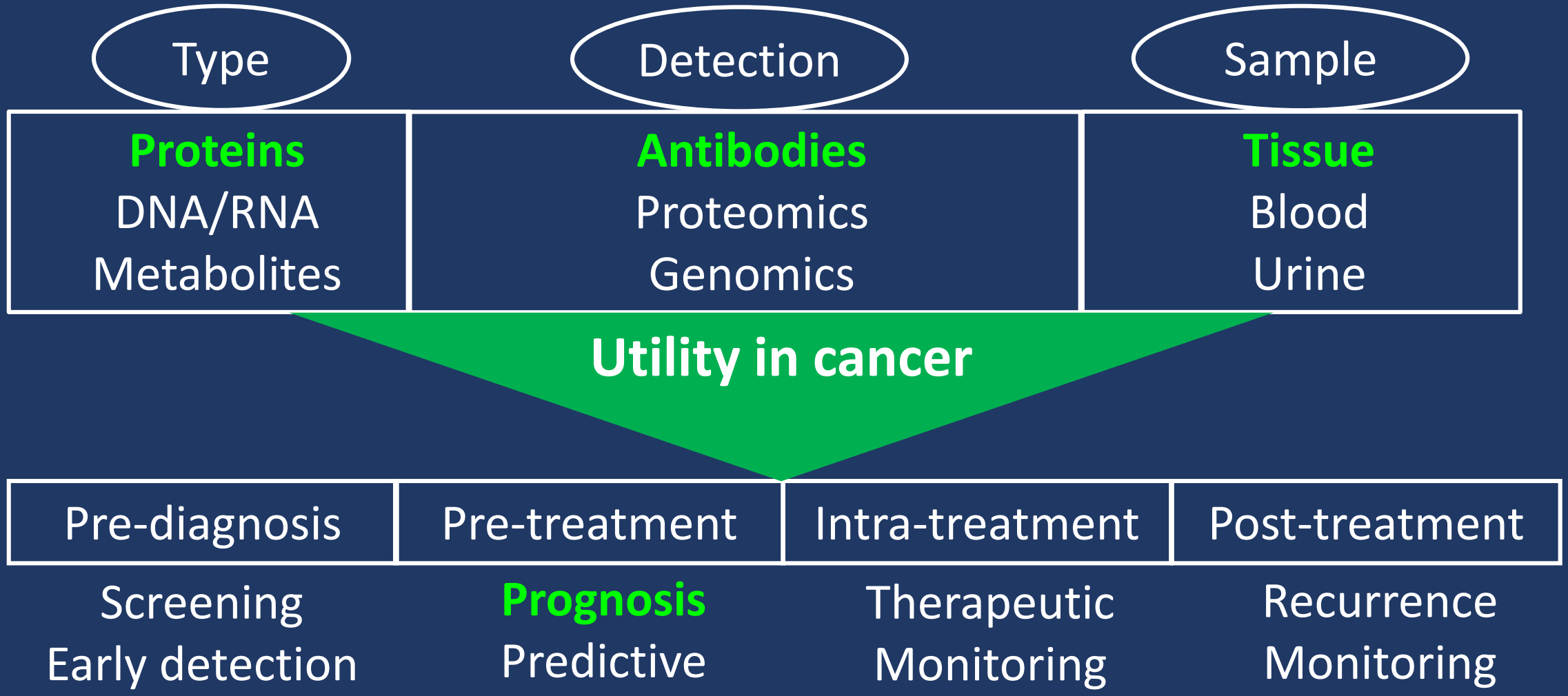
KTP Associate Conference 2019

Cancer

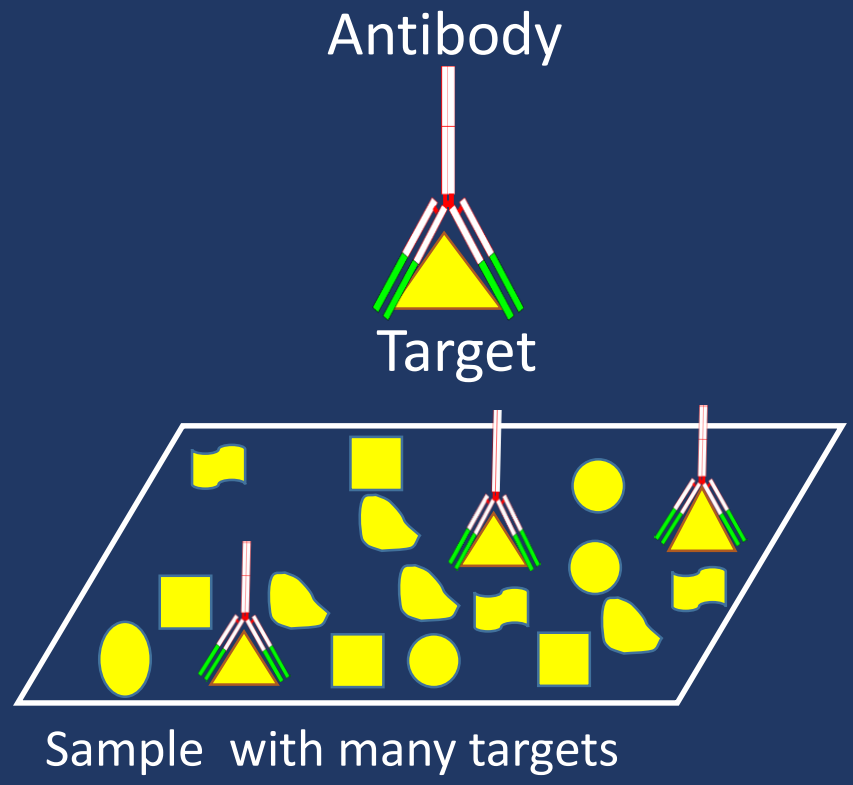
- Cancer is the second leading cause of death: Globally, about 1 in 6 deaths is due to cancer.
- Colorectal cancer is one of the most common types of cancer: around 1.36 million new cases are diagnosed each year.
- Colorectal cancer is the second leading cause of cancer related deaths.
- Improve survival rate through the identification of biomarkers.

Biomarkers


Type
Detection
Sample
Proteins
DNA/RNA
Metabolites
Antibodies
Proteomics
Genomics
Tissue
Blood
Urine
Utility in cancer
Pre-diagnosis
Pre-treatment
Intra-treatment
Post-treatment
Screening
Early detection
Prognosis
Predictive
Therapeutic
Monitoring
Recurrence
Monitoring

Monoclonal antibodies

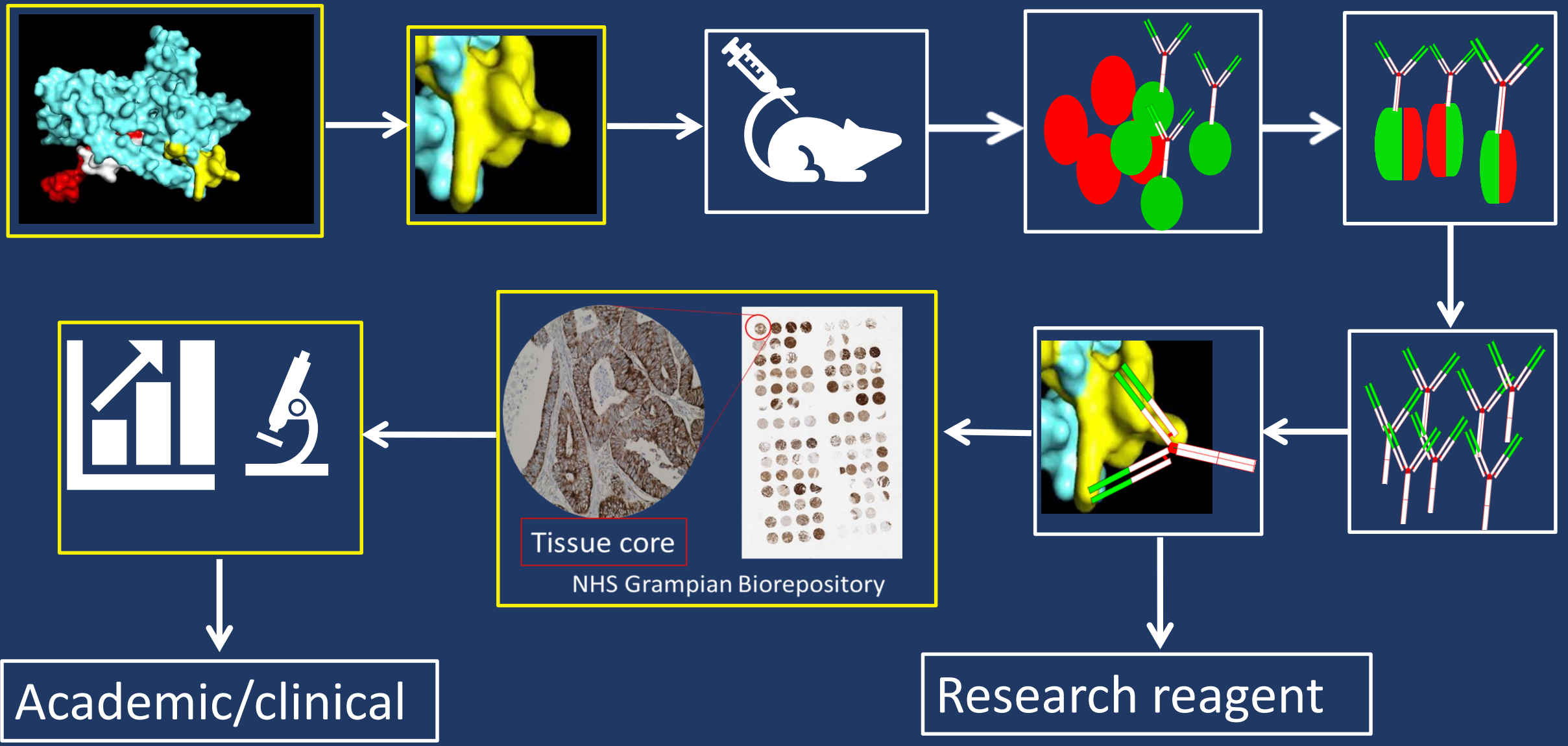
- Antibodies are biological probes that can recognise and bind to specific targets.
- Used in research and clinical assays and as therapeutic reagents.
- Global monoclonal antibodies market topped $100 billion in 2018.



Aims

- Identify novel protein targets associated with cancer development.
- Develop and characterise one antibody to each protein.
- Use the antibodies to evaluate their targets in colorectal cancer.
- Determine the clinical significance of each target as a biomarker.
- License antibodies/ targets as research reagents and/or as diagnostic tools.

Main steps


Tissue core
NHS Grampian Biorepository
Academic/clinical
Research reagent

Identification of targets

Online databases
Chromosomal locations

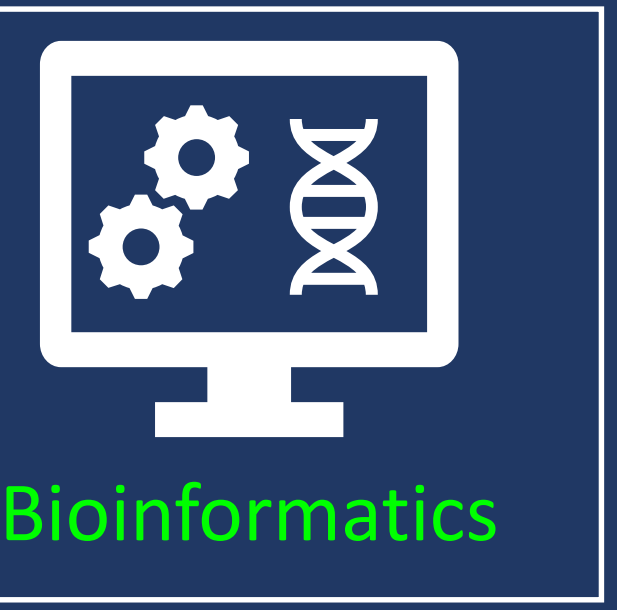
Primary list

Selection process

Novelty

Structure

Function

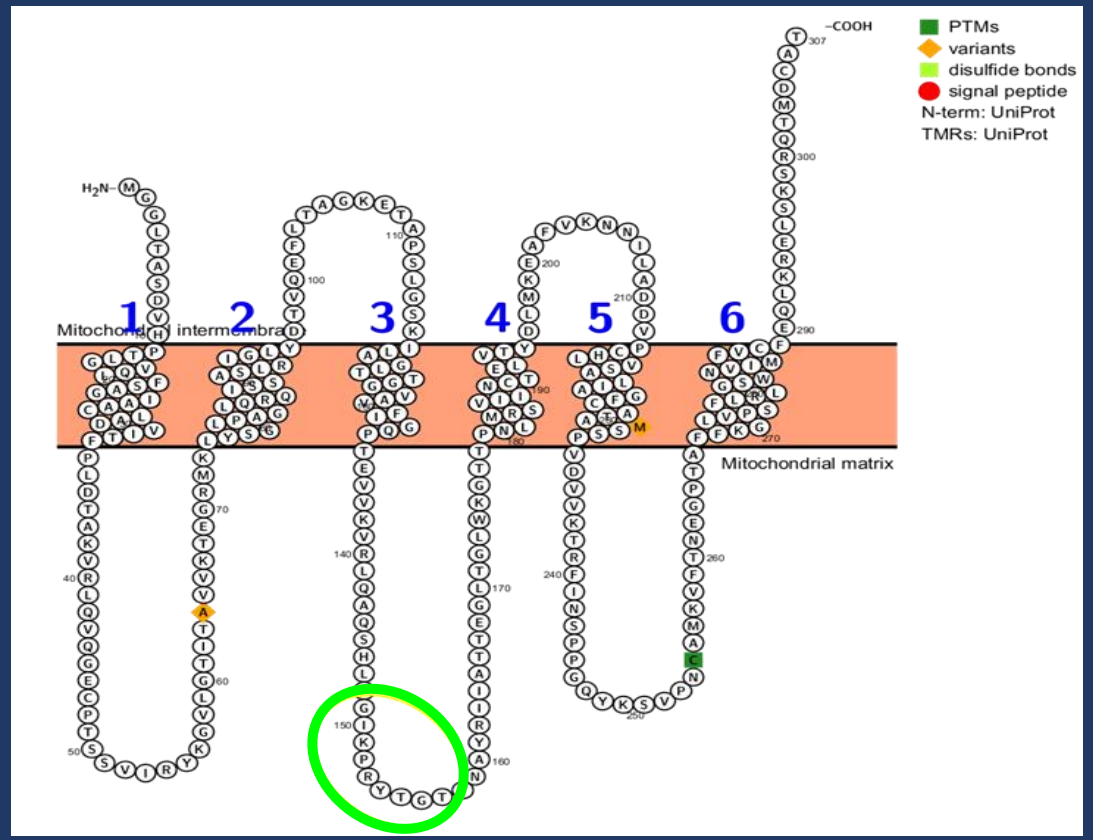


Bioinformatics

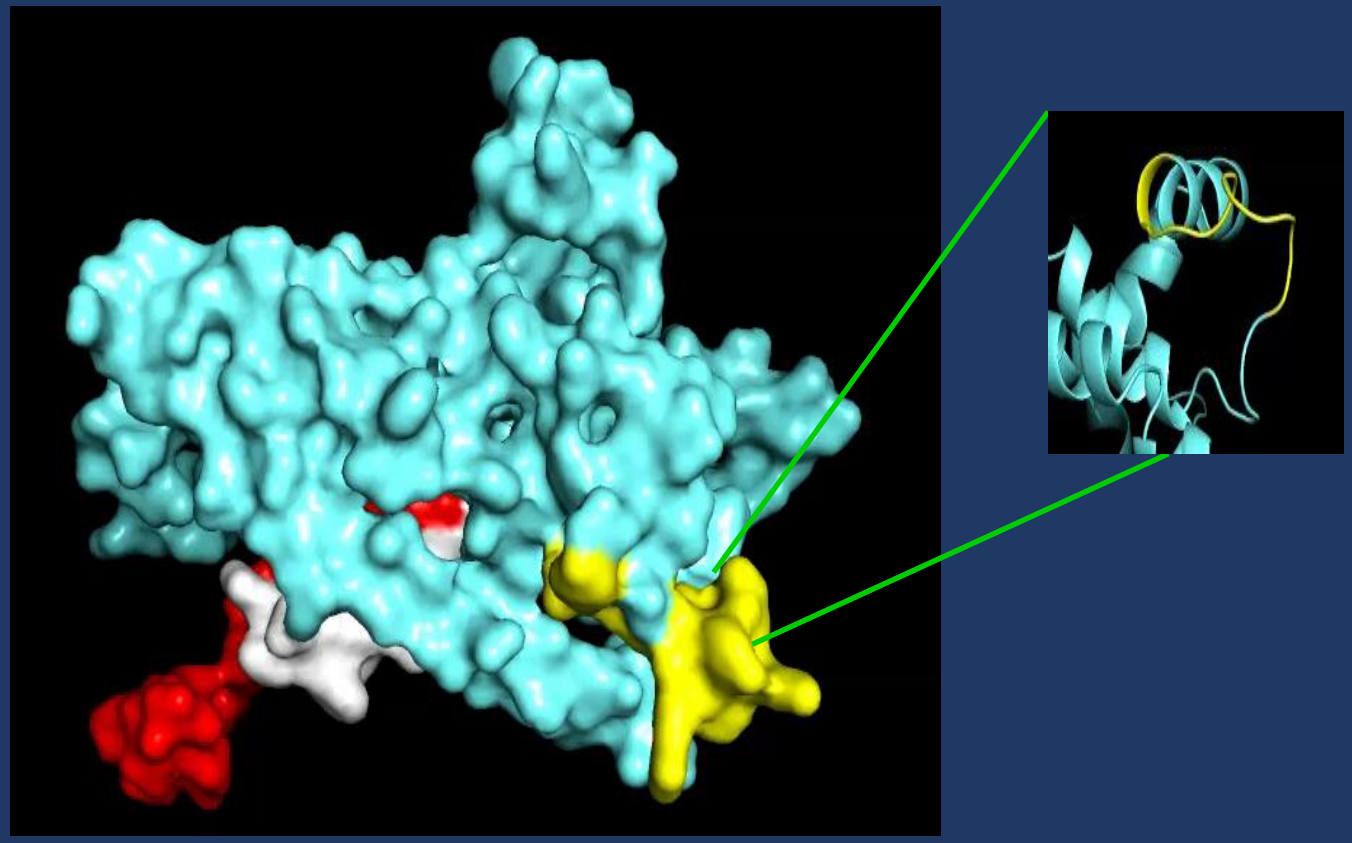
Targets (CIDEA, ELOVL3,ELOVL5 and UCP1)

Structural analysis

- Structural analysis:



Secondary structure of UCP1

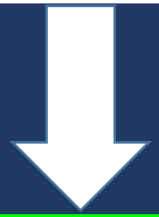


3D structure of UCP1

Peptide characteristics

- Key characteristics include hydrophilicity, antigenicity and specificity.
- Develop a model for peptide selection (database (n=250):

Peptides Sequence	Calculated parameters: length, weight, charge, etc	Immune response: negative, weak and strong



Peptide scoring system

Method-patient cohort

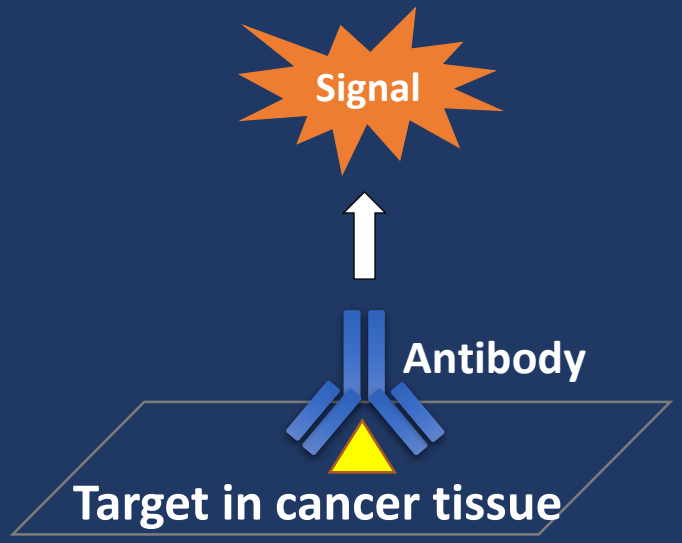
- Patients who had surgical resection of primary colorectal cancer at Aberdeen Royal Infirmary between 1994-2011 (n=823).

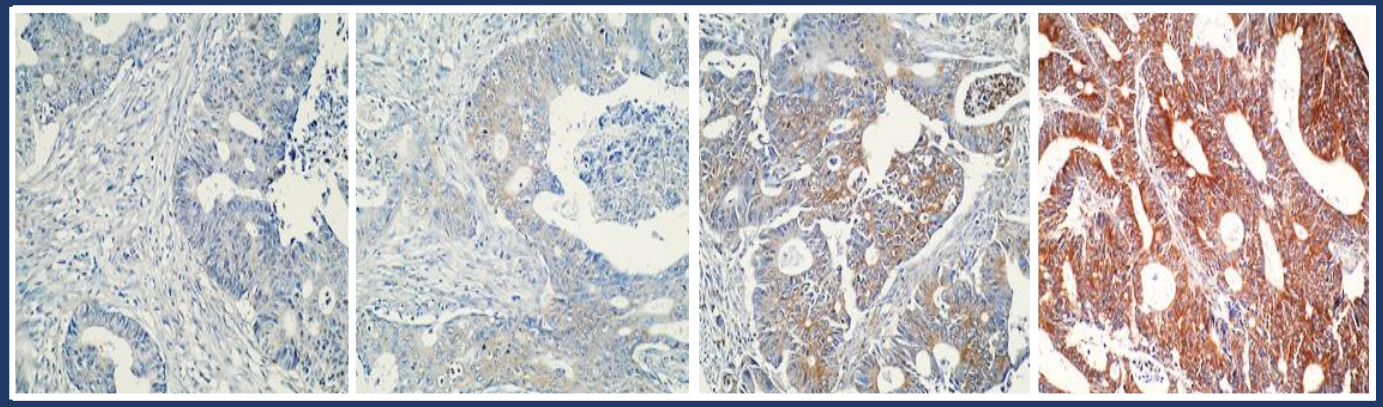
- Detailed clinicopathological characteristics for each patient.

- Tissue microarray:
  - High throughput analysis of multiple
  - specimens at the same time.
  - Standardisation and efficient use of resources.

NHS Grampian Biorepository

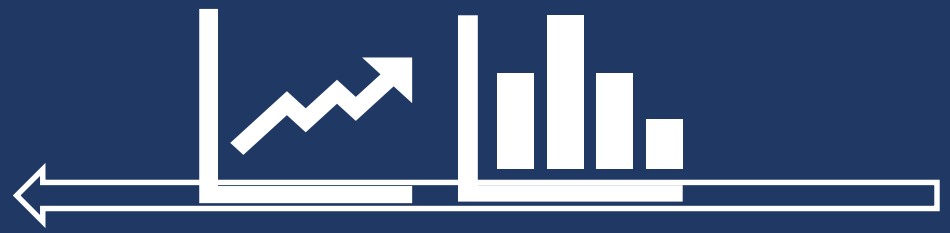
Method-Immunohistochemistry





Negative (0) Weak (1) Moderate (2) Strong (3)

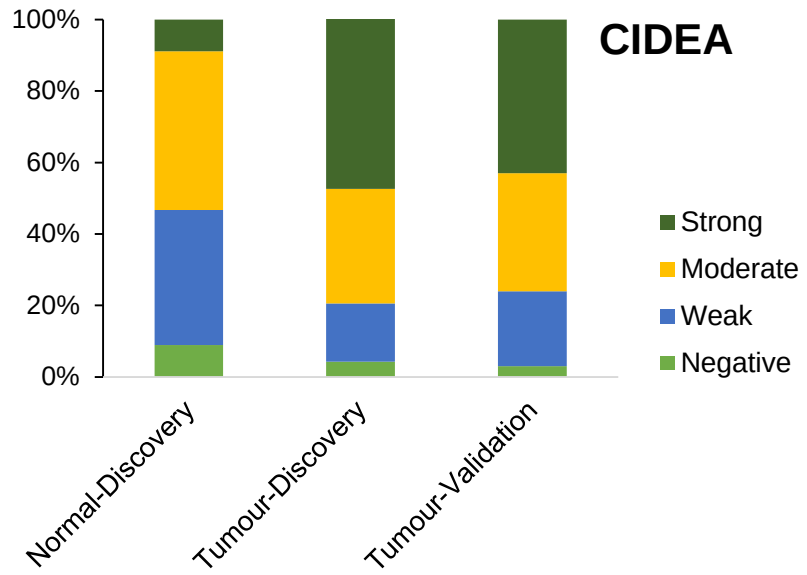
Cancer biomarker???

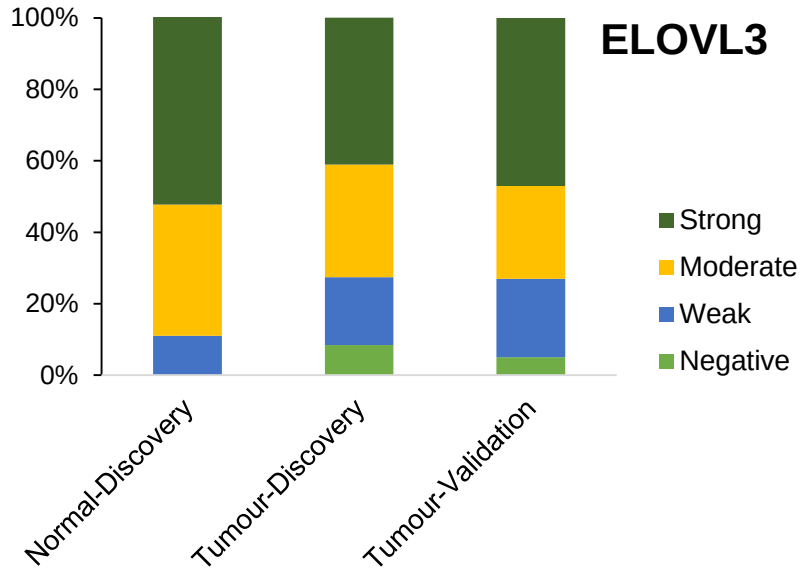


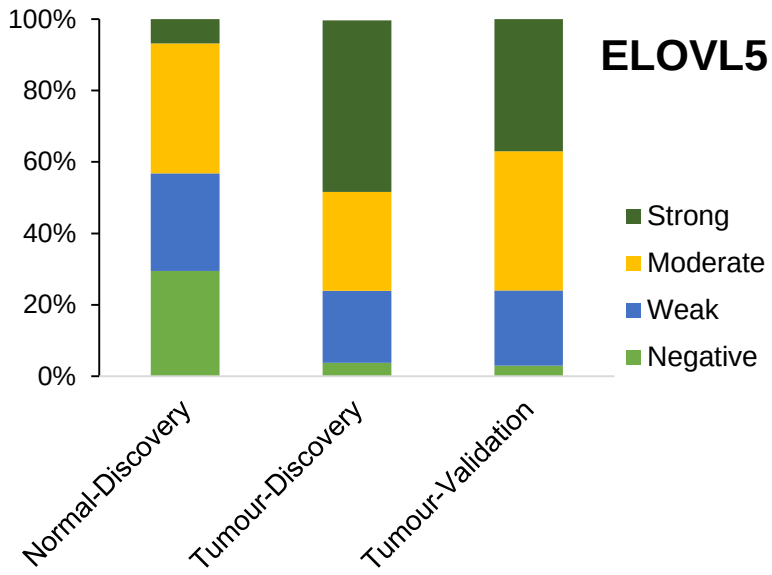
Datasheets
IBM SPSS

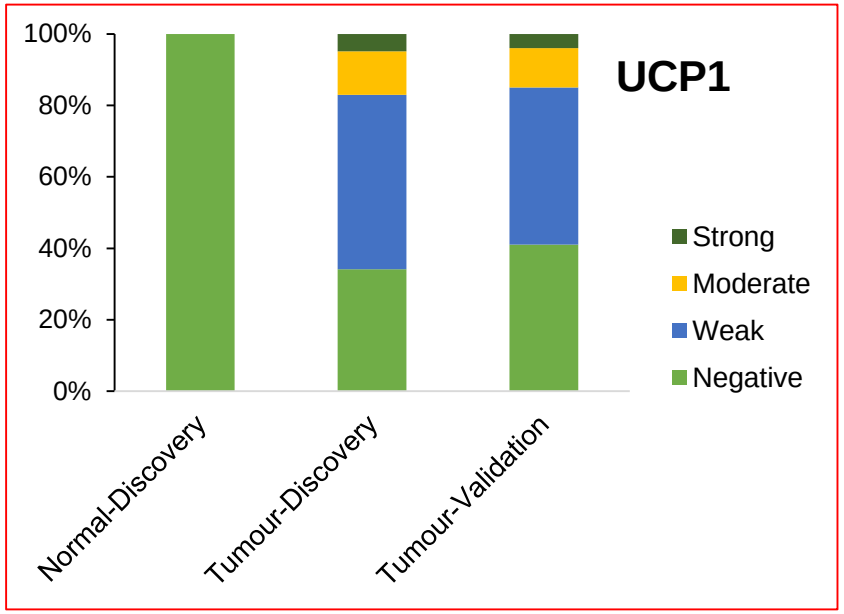
A Alnabulsi.*et al.* Int J Cancer. 2019. doi: 10.1002/ijc.32198.

Frequency distribution

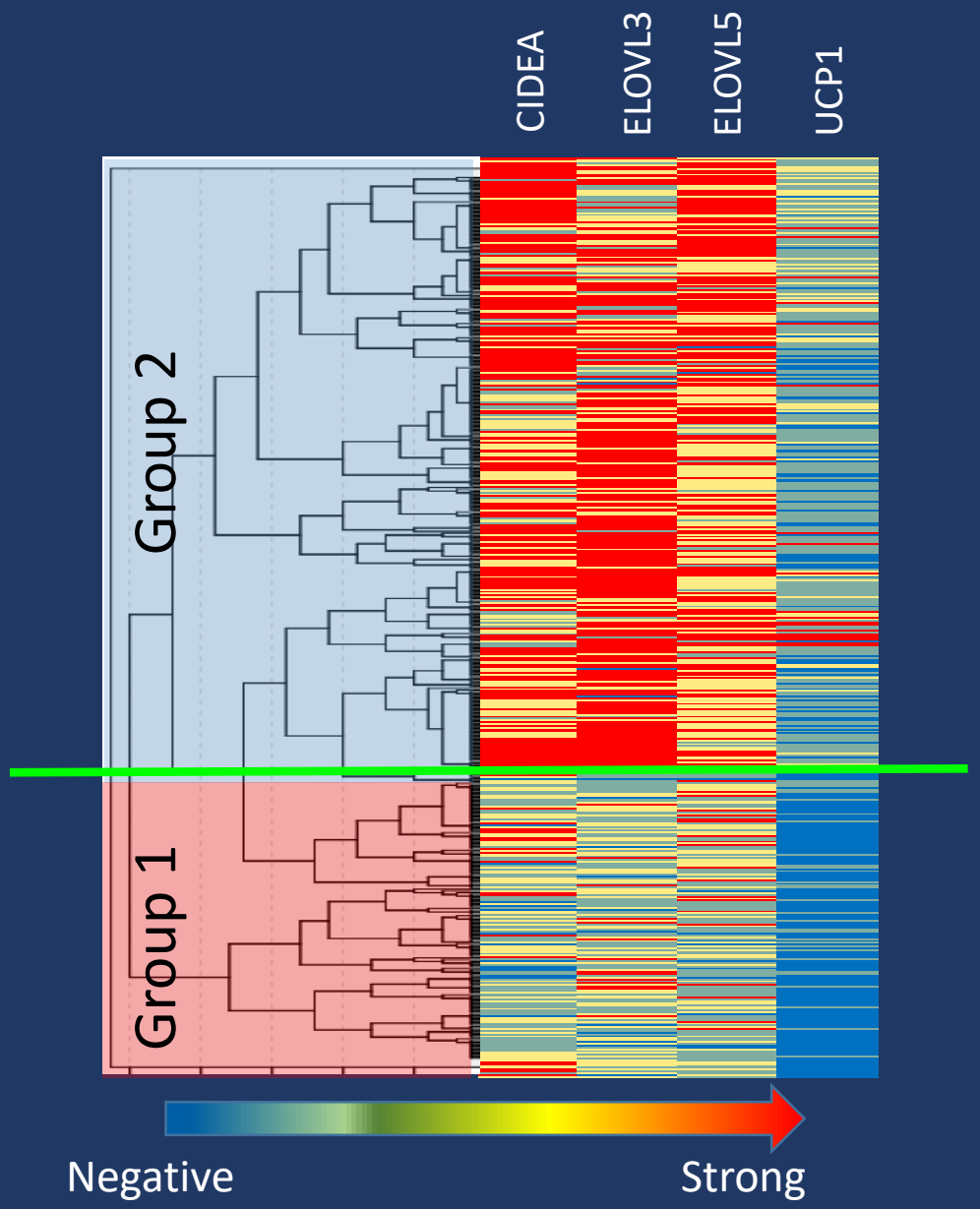


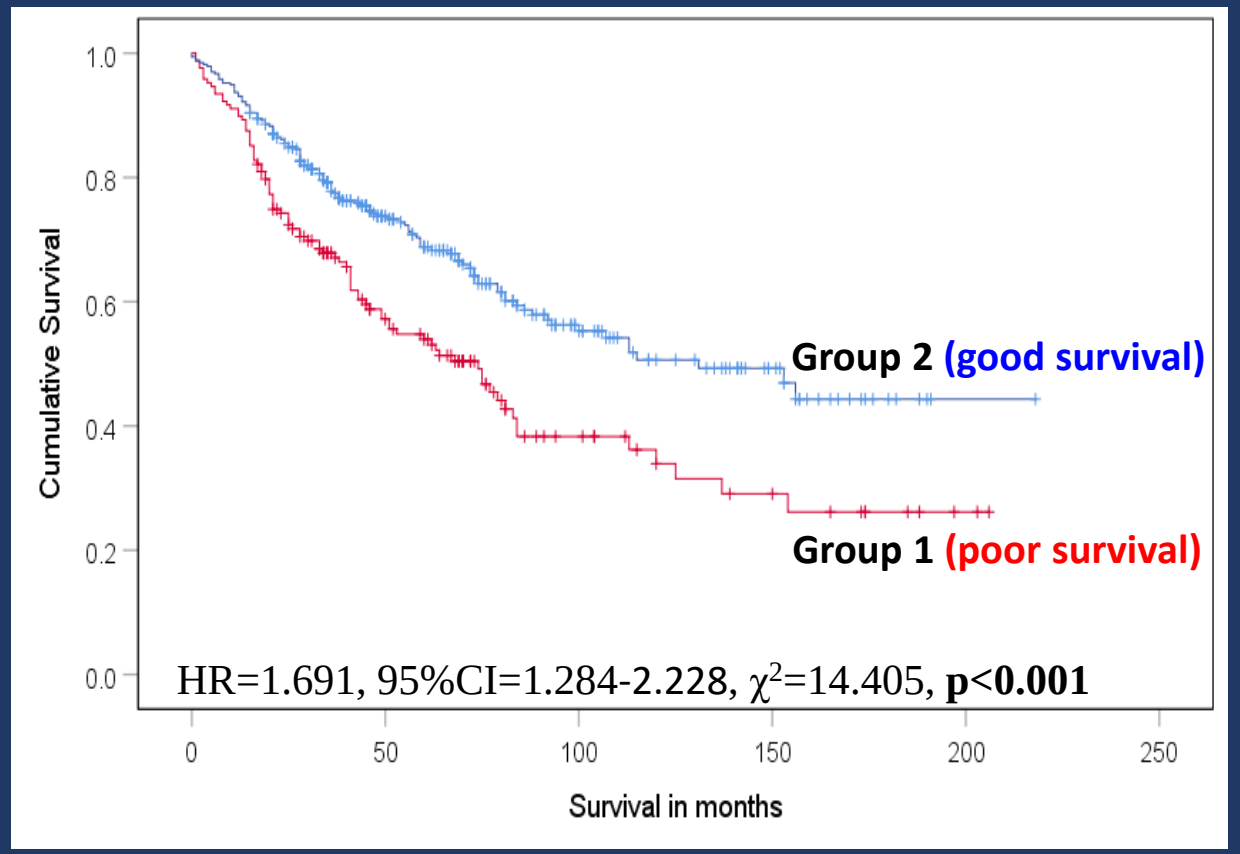






Cluster and survival analysis





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Acknowledgements

Innovate UK