A novel epigenetic immunoassay approach to profiling circulating nucleosomes for CRC

Dr Marielle Herzog
ESMO Poster Discussion session GI tumours, colorectal
Nucleosomes of tumor origin
- Nucleosomes are a basic structural unit for genes
- Nucleosome consist of DNA and histone proteins. Histones and DNA are subjected to a variety of **epigenetic modifications**
- Cell death results in fragmentation and release of nucleosomes into the blood
- Elevated cell turnover increases blood nucleosome levels (cancer, heart attack, surgery, severe autoimmune disease, inflammatory disease)
- ctDNA circulates as 160-80bp fragments bound to mononucleosomes and retains genetic mutations and epigenetic modifications of the cancer concerned
- Epigenetic changes in DNA & chromatin occurs early in tumorigenesis
- Nucleosomes inside diseased cells are characterized by unique epigenetic signatures

Nu.QTM assay
- Nu.QTM Tests Identify and Measure Circulating Nucleosome Structures for the Presence of Epigenetic Cancer Signals Within Blood
- ELISA immunoassay
- Small volume of blood required from patient (10ul in duplicate)
- Flexible to be run in any clinical setting: Manual ELISA, Automated system
Nucleosomes - Diagnostic Potential

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Colorectal Cancer (CRC)

CRC Screening program

- Screening for CRC currently involves faecal testing followed by colonoscopy for those with positive results.
- The most frequently used screening test across Europe is the faecal immunochemical test (FIT).
- This combination is effective at detecting cancer but:
  - Despite its high specificity (correct identification of healthy subjects), FIT test has a low sensitivity.
  - Less than 10% of people with a positive faecal test have a cancer.
- This means there are a significant number of unnecessary invasive and expensive colonoscopies performed and a long waiting list for colonoscopy.
- There is an urgent need to select sub-population for whom colonoscopy may be avoided.

447,136
New CRC cases in Europe per year

214,866
Number of deaths in Europe per year

148 million
Estimated screening population

2nd
Rank among all newly diagnosed cancers

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Normalized Nu.Q™ 5mC + FIT can reduce by 25% unnecessary colonoscopy whilst maintaining sensitivity for CRC.

Increasing CRC cases detected by 29% by increasing throughput of CRC screening.

For 1907 colonoscopy:
- 34 extra CRC cases detected.

Graph showing % of cases detected relative to present and % reduction in colonoscopies:
- **CRC**: 96.6% reduction at 10%, 88.5% reduction at 20%
- **High Risk Adenoma**

Bar chart showing number of CRC cases:
- Current FIT screening program
- Nu.Q™ + FIT
**FIT Positive**

- Patient with a positive FIT score could subsequently be given the blood based Nu.QTM test (an age–adjusted Nu.QTM assay for nucleosome associated with methylated DNA, normalised to total nucleosome) and then only be referred for colonoscopy if the combined test results indicate that is necessary.

- This combination of a Nu.QTM blood test + FIT score lead to:
  - Reduction by 25% of the number of unnecessary colonoscopies
  - Detection of 96,6% of FIT positive colorectal cancer cases
  - Increase FIT throughput by 33%
  - Net increase in total CRC cases detected by 29%

- Best outcome for most screening individuals

- The test will be CE marked by the end of 2016 and will be available for use in 2017

**Combination Nu.Q® blood test + FIT score**

- Less than 1 out of 10 have a cancer
- ~25% unnecessary colonoscopies
- Still detection of ≈ 97% of CRC cases

**Nu.QTM + FIT**

- Colonoscopy

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Colonoscopy

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