

Sex-specific panel of 10 proteins can pick up 18 different early stage cancers

Could kickstart new generation of screening tests for early cancer detection, say researchers

A sex-specific panel of 10 proteins can pick up 18 different early stage cancers, representing all the major organs of the human body, finds a proof of concept study published in the open access journal ***BMJ Oncology***.

The findings could kick-start a new generation of screening tests for early detection of the disease, say the researchers, particularly as there are many sex specific differences in cancer—including age at occurrence, cancer types, and genetic alterations—points out a linked editorial.

Cancer accounts for 1 in every 6 deaths around the globe, with nearly 60% of these deaths caused by cancers for which no screening test exists, note the researchers.

What's more, even existing screening tests have considerable drawbacks, including invasiveness, expense, and low levels of accuracy for early stage disease, they add.

Specific blood proteins could be used for early detection and ongoing monitoring, but the currently available options lack sensitivity—accuracy of picking up those with cancer—and specificity—accuracy of excluding those without cancer, say the researchers.

To explore the potential use of plasma proteins, including those that are currently barely detectable, as biological signatures of solid tumours in specific organs, the researchers collected plasma samples from 440 people diagnosed with 18 different types of cancer before treatment, and from 44 healthy blood donors.

They then measured more than 3000 proteins strongly associated with cancer chemical pathways in each sample, using a technology deploying antibodies and a statistical algorithm in a 2-step process.

The first step involved detecting the biological signature of any cancer, and the second step involved identifying the tissue of origin and cancer subtypes—small cell and non-small cell cancers of the lung, for example.

Through a process of elimination, a panel of 10 sex specific proteins emerged that were differentially expressed among the plasma samples from cancer patients and healthy people.

The fact that these protein signatures differed significantly between men and women suggests that they are most likely sex-specific for all cancers, say the researchers.

By themselves, each individual protein was only moderately accurate at picking up early stage disease, but when combined with the other proteins in a panel they were highly accurate.

These proteins were able to pick up stage I-III disease and all types of cancer, but were particularly effective at picking up early stage disease.

They identified 93% of stage 1 cancers among the men and 84% of stage 1 cancers among the women, with 99% specificity and 90% sensitivity in the men and 85% sensitivity and 99% specificity in the women.

A panel of 150 proteins were able to identify the tissue of origin of most cancers in more than 80% of cases in both men and women.

Analysis of the plasma protein amounts showed that almost all of them were present at very low levels, highlighting the importance of low-level proteins to pick up pre-cancerous and early stage disease before a tumour has yet to have any substantial systemic impact, say the researchers.

They acknowledge the relatively small sample size of their study and the lack of information on co-existing conditions, potentially limiting the wider applicability of their findings. And despite advancements in proteomic techniques, the full range of proteins produced by a particular cell or organ isn't yet known, they add.

Nevertheless they conclude: "Our new generation protein-based plasma test has shown high sensitivity in detecting a variety of early stage tumours in asymptomatic patients, making it a strong candidate for use as a population-wide screening tool that is not currently achievable with existing tests or techniques."

In a linked editorial, Dr Holli Loomans-Kropp, of the College of Medicine, The Ohio State University, adds: "Although several problems need to be addressed before MCED [multi-cancer early detection] tests can be deployed at a population scale, a method to improve on current issues of sensitivity and specificity may be use of sex-specific detection panels."

She continues: "Demonstrable sex-specific differences in cancer—including age of onset, cancer types and genetic alterations—suggest this approach would be useful.

"The widespread use of MCEDs may be a way down the road, but perhaps employing a strategy like sex-specific MCED panels could get the field moving a little faster."