Molecular biomarkers for cervical cancer

With half a million new cases every year, cervical cancer is the fourth most common cancer affecting women worldwide. The introduction of improved diagnostic tools and new biomarkers should facilitate cervical screening in the post human papilloma virus (HPV) vaccination era.

Cervical cancer is usually preceded by a long phase of pre-invasive disease called cervical intraepithelial neoplasia (CIN). Cervical cytology and HPV screening are standard practice in cervical screening for assessment of risk of developing CIN, while histology is the gold standard for disease diagnosis. With the introduction of HPV vaccination, the landscape of cervical pre-cancer will change over time. While the incidence of abnormal smears and high grade disease will decrease over time, the lower prevalence of disease will directly impact on the performance characteristics of current diagnostic tests. There is a need for alternative approaches and specific biomarkers to aid in screening for and objective CIN lesion grading.

The scope of the EU-funded SYSTEMCERV (Systems biology approaches to cervical pre-cancer and cancer) project was to develop and validate a protein biomarker array for diagnosing cervical cancer as well as pre-cancerous lesions. SYSTEMCERV is a continuation of the project AUTOCAST, where a novel panel of RNA-based biomarkers for detection of cervical pre-cancerous lesions were identified. This particular biomarker panel had a specificity of 93% and sensitivity of 88 % for detecting CIN 2-3 lesions.

The SYSTEMCERV partners wished to extend this work and use systems biology approaches to derive novel biomarkers and gain more in depth understanding of the underlying pathways involved in the carcinogenic process. Using signal transduction pathway profiling, the team discovered pathways implicated in HPV and cervical carcinogenesis (p53, SMAD, STAT) as well as novel pathways. Furthermore, through next generation sequencing they identified genes with a higher mutation risk in cervical pre-cancer.

Bioinformatics analysis of specific transcription factor-gene interactions led to the discovery of three promising biomarkers (CXCL13, DSG3 and TP63), which the scientists took forward within the project. Following extensive clinical validation on over 100 pre-cancer/cancer cases, they exhibited promising results as markers of CIN and CIN progression.

The SYSTEMCERV team aimed to take their diagnostic approaches a step further by using systems biology approaches to develop protein arrays for CIN and cervical cancer diagnosis. In this context, they developed and characterised an integrated demonstrator device incorporating proto-arrays and label free detection technology. This was achieved using a revolutionary microfluidic DNA-to-protein copying technology. For detection of proteins, the consortium used label-free biosensor technology based on reflectometric interference spectroscopy.
Collectively, the SYSTEMCERV work resulted in significant innovations in the field of cervical cancer and pre-cancer diagnosis. Given that detection accurate grading of CIN lesions is paramount for clinical management of patients, the generated tools should facilitate appropriate and prompt treatment.

**Related information**

| Report Summary | Final Report Summary - SYSTEMCERV (Systems biology approaches to cervical pre-cancer and cancer) |

**Subjects**

Scientific Research

**Keywords**

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