Researcher Profile

UHN Microarray Centre

Dr. Nicole Clarke

Elucidating the mechanism of IRF-1 in tumour suppression

In order to prevent cancerous tumours from developing, a better understanding of the mechanisms that control tumour suppressor proteins is required. The Interferon Regulatory Factor (IRF) family of proteins harbour tumour suppressor activity in a number of cancer cell systems and are potential targets for cancer therapy. Much of Dr. Clarke's research focuses on the tumour suppressor/transcription factor IRF-1. By combining several techniques, including ChIP-chip, global transcript profiling, and cellular studies, a comprehensive network of the tumour suppressor activity of IRF-1 will be defined.

In 2004, Dr. Clarke and Dr. Gronemeyer identified the Tumour Necrosis Factor-Related Apoptosis-Inducing Ligand (TRAIL)-mediated tumour suppressor activity of IRF-1. This study found that in both acute promyelocytic leukemia and breast cancer cells retinoic acid-induced IRF-1 causes TRAIL promoter activation (1). Dr. Clarke's research is now focused on the identification of the transcriptional networks associated with IRF-1. In a recent study, Dr. Clarke and her colleagues identified 200 new IRF1-binding sites by performing chromatin immunoprecipitation followed by hybridisation to UHNMAC Human 12K CGI microarrays (2). This data provides a more complete understanding of the regulatory networks controlled by IRF-1 and reveals a novel role for IRF-1 in regulating the interstrand crosslink DNA damage response.

Dr. Clarke is also investigating the role of post-transcriptional modifications in the regulation of IRF-1 and identifying proteins that interact with IRF-1 and control its expression. The ultimate goal of these studies is to better understand the mechanisms involved in IRF tumour suppressor activity and thus, to identify new ways to therapeutically target IRFs for cancer therapy.

Dr. Nicole Clarke is a Lecturer in Gene Regulation at the School of Pharmacy, University of Nottingham, U.K.

References:

1. Clarke N, *et al*. Tumor suppressor IRF-1 mediates retinoid and interferon anticancer signaling to death ligand TRAIL. EMBO J 2004, 23:3051
2. Frontini M, *et al*. A ChIP-chip approach reveals a novel role for transcription factor IRF1 in the DNA damage response. Nucleic Acids Res 2009, 37(4):1073

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