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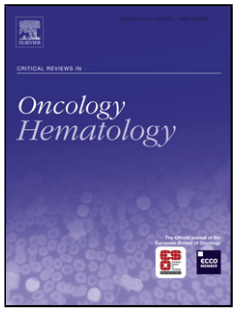

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UNRAVELLING THE COMPLEXITY OF SIGNALLING NETWORKS IN CANCER: A REVIEW OF THE INCREASING ROLE FOR COMPUTATIONAL MODELLING.

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ABSTRACT

Cancer induction is a highly complex process involving hundreds of different inducers but whose eventual outcome is the same. Clearly, it is essential to understand how signalling pathways and networks generated by these inducers interact to regulate cell behaviour and create the cancer phenotype. While enormous strides have been made in identifying key networking profiles, the amount of data generated far exceeds our ability to understand how it all "fits together". The number of potential interactions is astronomically large and requires novel approaches and extreme computation methods to dissect them out. However, such methodologies have high intrinsic mathematical and conceptual content which is difficult to follow. This review explains how computation modelling is progressively finding solutions and also revealing unexpected and unpredictable nano-scale molecular behaviours extremely relevant to how signalling and networking are coherently integrated. It is divided into linked sections illustrated by numerous figures from the literature describing different approaches and offering visual portrayals of networking and major conceptual advances in the field. First, the problem of signalling complexity and data collection is illustrated for only a small selection of known oncogenes. Next, new concepts from biophysics, molecular behaviours, kinetics, organisation at the nano level and predictive models are presented. These areas include:

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