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0607 CAMBRIDGE INTERNATIONAL MATHEMATICS

0607/41

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S1 Jan 2014 Mark Scheme

P. Clavin



S1 Jan 2014 Mark Scheme:

The Pall Mall Budget, 1886 Quantitative Assessment and Validation of Network Inference Methods in Bioinformatics

Benjamin Haibe-Kains, Frank Emmert-Streib, 2015-04-14 Scientists today have access to an unprecedented arsenal of high tech tools that can be used to thoroughly characterize biological systems of interest. High throughput omics technologies enable to generate enormous quantities of data at the DNA, RNA, epigenetic and proteomic levels. One of the major challenges of the post genomic era is to extract functional information by integrating such heterogeneous high throughput genomic data. This is not a trivial task as we are increasingly coming to understand that it is not individual genes but rather biological pathways and networks that drive an organism's response to environmental factors and the development of its particular phenotype. In order to fully understand the way in which these networks interact or fail to do so in specific states, disease for instance, we must learn both the structure of the underlying networks and the rules that govern their behavior. In recent years there has been an increasing interest in methods that aim to infer biological networks. These methods enable the opportunity for better understanding the interactions between genomic features and the overall structure and behavior of the underlying networks. So far such network models have been mainly used to identify and validate new interactions between genes of interest. But ultimately one could use these networks to predict large scale effects of perturbations such as treatment by multiple targeted drugs. However currently we are still at an early stage of comprehending methods and approaches providing a robust statistical framework to quantitatively assess the quality of network inference and its predictive potential. The scope of this Research Topic in Bioinformatics and Computational Biology aims at addressing these issues by investigating the various complementary approaches to quantify the quality of network models. These validation techniques could focus on assessing quality of specific interactions, global and local structures and predictive ability of network models. These methods could rely exclusively on in silico evaluation procedures or they could be coupled with novel experimental designs to generate the biological data necessary to properly validate inferred networks. **Oswaal CBSE**

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initially confined to the regulation of tryptophan availability in local tissue microenvironments is now considered to play a wider role that extends to homeostasis and plasticity of the immune system Thus IDO biology has implications for many aspects of immunopathology including viral infections neoplasia autoimmunity and chronic inflammation Its immunoregulatory effects are mainly mediated by dendritic cells DCs and involve not only tryptophan deprivation but also production of kynurenines that act on IDO DCs thus rendering an otherwise stimulatory DC capable of regulatory effects as well as on T cells The aryl hydrocarbon receptor AhR is a ligand operated transcription factor originally recognized as the effector mediating the pathologic effects of dioxins and other pollutants However it is now well established that AhR activation by endogenous ligands can produce immunoregulatory effects The IDO1 mechanism appears to have been selected through phylogenesis primarily to prevent overreacting responses to TLR recognized pathogen associated molecular patterns and only later did it become involved in the response to T cell receptor recognized antigens As a result in mammals IDO1 has become pivotal in fetomaternal tolerance at a time when regulatory T cells emerged to meet the same need namely protecting the fetus IDO1 and regulatory T Treg cells may have then coevolved to broaden their function well beyond their initial task of protecting the fetus such that in acquired immunity IDO1 with its dual enzymic and signaling function has turned into an important component of the peripheral generation and effector function of regulatory T cells AhR in turn which has a role in regulatory T cell generation is presumed to have evolved from invertebrates where it served a ligand independent role in normal development processes Evolution of the receptor in vertebrates resulted in the ability to bind structurally different ligands including xenobiotics and microbiota derived catabolites Considering the inability of invertebrate AhR homologs to bind dioxins the adaptive role of the AhR to act as a regulator of xenobiotic metabolizing enzymes may have been a vertebrate innovation to later acquire an additional immune regulatory role by coevolutionary pressure in mammals by IDO1 and regulatory T cells Thus an entirely new paradigm in immunology and more specifically in immune tolerance is the coevolution of three systems namely the IDO1 mechanism AhR driven gene transcription and T cell regulatory activity that originating from the initial need of protecting the fetus in mammals have later turned into a pivotal mechanism of peripheral tolerance in autoimmunity transplantation and neoplasia

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