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HUMAN DISEASE

Cell types in profile

The breakdown of functions that are specific to particular cell types is central to many diseases. Transcriptional profiling is a potentially powerful method to study this malfunctioning, but it is often impossible to isolate individual cell types for such analyses. A computational approach has now been developed to overcome this problem by inferring cell type-specific expression from whole-tissue samples.

Ju *et al*. devised a method called '*in silico* nano-dissection', which uses machine learning. The approach utilizes known cell-lineage markers and looks at their expression in different conditions using microarray data from whole-tissue homogenates. These patterns are then used to infer other cell type-specific genes from expression data.

The authors used this method to identify genes that are expressed specifically in podocytes — cells that malfunction in kidney diseases. Using expression data from kidney biopsy samples, they identified 136 genes as new candidates for podocyte-specific expression. Immunohistochemical staining confirmed that a large proportion of genes identified are indeed specific to this lineage. Importantly, these predictions are more accurate than those identified experimentally in a mouse model.

Two of the identified genes have been shown to have roles in kidney disease, which suggests that this approach will be useful for identifying other disease genes. Furthermore, the expression patterns of the podocyte-specific genes correlate with the extent of renal malfunction in patients.

The authors show that their approach can also be used for other cell lineages, suggesting its applicability to a wide range of diseases, as well as to normal physiology.

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ORIGINAL RESEARCH PAPER Ju, W. *et al*. Defining cell-type specificity at the transcriptional level in human disease. *Genome Res*. http://dx.doi.org/10.1101/gr.155697.113 (2013)