Predicting eukaryotic protein secretion without signals

Predicting unconventional protein secretion is a much harder problem than predicting signal peptide-based protein secretion, both due to the small number of examples and due to the heterogeneity and the limited knowledge of the pathways involved, especially in eukaryotes. However, the idea that secreted proteins share certain properties regardless of the secretion pathway used made it possible to construct the prediction method SecretomeP in 2004. Here, we take a critical look at SecretomeP and its successors, and we also discuss whether multi-category subcellular location predictors can be used to predict unconventional protein secretion in eukaryotes. A new benchmark shows SecretomeP to perform much worse than initially estimated, casting doubt on the underlying hypothesis. On a more positive note, recent developments in machine learning may have the potential to construct new methods which can not only predict unconventional protein secretion but also point out which parts of a sequence are important for secretion.

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