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Editorial

Secretomics: Type of Proteomics which Involves the Analysis of the Secretome

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EDITORIAL NOTE

Secretomics is a branch of proteomics that examines a cell's, tissue's, or organism's secretome—all of its secreted proteins. Secreted proteins play a role in a range of normal functions, such as cell communication and matrix remodelling, but they are also essential for malignant cell invasion and metastasis. Secretomics has thus played a critical role in the discovery of cancer biomarkers and the understanding of the molecular basis of disease. Matrisomics is the study of the insoluble part of the secretome.

In their investigation of *the eubacterium B. subtilis*, Tjalsma et al. developed the term "secretome." The secretome was defined as all of the bacteria's secreted proteins and secretory apparatus. They were able to predict what fraction of the proteome is secreted by the cell using a database of *B. subtilis* protein sequences and an algorithm that looked at cleavage sites and amino-terminal signal peptides indicative of secreted proteins. The same lab established a standard for secretomics in 2001, demonstrating that predictions based on amino acid sequence alone are insufficient to define the secretome. They identified 82 proteins released by *B. subtilis* using two-dimensional gel electrophoresis and mass spectrometry, only 48 of which had been predicted using their earlier genome-based technique. This emphasises the importance of protein confirmation of projected results. Because of the intricate nature of secretory routes there are many non-classical secretion pathways, as well as many non-secreted proteins that are a member of the classical secretory pathway a more detailed definition of the secretome was required. Agrawal et al. proposed defining the secretome as "the global group of secreted proteins into the extracellular space by a cell, tissue, organ, or organism at any given time and under any given condition through known and unknown secretory mechanisms involving constitutive and regulated secretory organelles through known and unknown secretory mechanisms involving constitutive and regulated secretory organelles."

Many secreted proteins have an N-terminal peptide sequence that instructs the translated protein to proceed to the endoplasmic reticulum, where it is processed before being secreted. The existence of these signal peptides can help anticipate a cell's secretome. SignalP, for example, can recognise signal sequences and predict secreted proteins. Because transmembrane proteins are processed but not secreted in the ER, software such as the TMHMM server is used to predict transmembrane domains and thereby eliminate false positives.

Classic signal peptide sequences are absent from several secretory proteins. SignalP will miss these 'leaderless secretory proteins' (LSPs). SecretomeP is a piece of software that attempts to predict non-classical secretory proteins based on their sequences. A vast range of creatures, including humans, mice, zebrafish, and hundreds of bacteria, have been predicted to have genome-wide secretomes. There are a number of issues with genome-wide prediction systems. There's a good chance you'll get false positives and false negatives. Furthermore, because gene expression is significantly impacted by environmental factors, a secretome predicted from the genome or a cDNA library is unlikely to match the genuine secretome perfectly. To confirm any anticipated secreted proteins, proteomic methods are required. On the basis of both curation and computational prediction, several genome-wide secretome databases or knowledgebase are available. The fungal secretome database (FSD), the fungal secretome knowledgebase (FunSecKB), and the lactic acid bacterial secretome database are among these databases. MetaSecKB, a database of human and animal protein subcellular locations, and ProtSecKB, a database of protist subcellular proteomes, were both recently released. These databases are useful resources for further describing protein subcellular locations, notwithstanding certain flaws in the computer prediction.

Secretomics relies heavily on mass spectrometry analysis. A protease is used to degrade serum or supernatant containing secreted proteins and the proteins are sorted using 2D gel electrophoresis or chromatographic techniques. Each protein is then evaluated using mass spectrometry, and the peptide-mass fingerprint created can be used to identify the protein using a database.

In secretomics, stable isotope labelling by amino acids in cell culture (SILAC) has emerged as a useful tool for distinguishing

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secreted proteins from bovine serum impurities in cell culture. The supernatant from cells grown in normal medium and cells grown in medium with stable-isotope labelled amino acids is combined 1:1 and evaluated by mass spectrometry. Because there is no labelled equivalent for protein contaminants in serum, there will only be one peak. The SILAC approach, for example, has been effectively employed to differentiate between proteins released by human chondrocytes in vitro and serum pollutants.