A Central Resource for Platelet Proteomics

Gerard Cagney, James McRedmond

An impressive but bewildering array of data are now available, at the touch of a button, for every gene and protein in the human body. This information is the harvest of the so-called “omics” technologies, which began with the human genome sequencing project and gained from subsequent efforts to characterize the transcriptome, proteome, and metabolome of individual cell types. Those coming from the perspective of vascular biology, however, might ask how does one begin to use this information to gain deeper insights into disease? In this issue of Arteriosclerosis, Thrombosis, and Vascular Biology, Dittrich and coworkers describe a database, PlateletWeb, that goes some way toward meeting that need.

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In the last 5 years, our baseline knowledge of the core components of human platelets has expanded considerably. Several key studies have described the mRNA species found in platelets.1-4 Because the proteome is reflected in the transcriptome,5 these studies represent a catalogue of potential platelet proteins. In addition, selected platelet messages are translated into protein after activation, regulating the inflammatory and hemostatic responses of the platelet.6,7 Thus, the platelet transcriptome, inherited from precursor megakaryocytes, both reflects and affects platelet function. Indeed, comparative transcriptional studies have revealed differences in the platelet make-up between sexes8 and in disease states.9 Because drug treatments for hypertension can result in changes in megakaryocyte ploidy and platelet size10 and alter the platelet proteome,11 understanding the regulation of platelet messages and their translation—in the platelet and the megakaryocyte—may lead to better treatments for cardiovascular disease.

Similarly, recent work has greatly increased our knowledge of the platelet proteome. Taking advantage of recent developments in protein mass spectrometry, key 2-dimensional gel studies12-14 were followed by analyses using orthogonal chromatographic methods.15 Further work focused on subproteomes: the platelet membrane,16 the microparticle,17 the releasate,18 A number of groups have attempted to identify platelet phosphoproteins.19,20

All this represents the baseline machinery—the individual mRNA and protein species present in a platelet cell—that platelets must use to deliver their multiple functions. The challenge is to learn how these units interact, and two questions arise. First, which components are platelet-specific and second, conversely, which pathways and complexes are shared with other cells. In the latter case, we need to determine whether they are carrying out the same function in each cell type. By addressing these questions, we can begin to formulate models of how platelets work and perhaps, ultimately, propose more effective platelet-specific therapies.

The revolution in platelet functional genomics has been paralleled in other fields, and there is now a wealth of data describing features of all genes and proteins that can give clues to their biological function—biophysical properties such as the presence of domains, posttranslation modifications (eg, SwissProt); biochemical properties such as protein-protein interactions (eg, the Database of Interacting Proteins, DIP); genetic evidence for the roles of genes and proteins in pathways (eg, Kyoto Encyclopedia of Genes and Genomes, KEGG). There is also a vast literature describing individual biochemical studies (PubMed), and much of this has been encapsulated into hierarchical and ontological databases such as GO (eg, Gene Ontology).

Where to begin to untangle this data for an individual cell such as a platelet? Here, Dittrich et al have done the field a major service by generating a database of platelet functional genomics knowledge. The website houses what is effectively a “virtual platelet.” The database contains the primary “omics” data in a centralized and easy-to-use website (http://plateletweb.bioapps.biozentrum.uni-wuerzburg.de). However, the authors go considerably further by annotating this with information on protein domains, functions etc, and importantly, they establish connections between platelet proteins via reported interactions from other cells.

This effort is somewhat pioneering, with few comparable examples for other cell types. However, one can imagine an emerging network of such databases, each focusing on a single cell or tissue type that would allow a powerful comparison of cell components and behaviors. This will be important for understanding the specific functions of a given cell. Blood cells frequently interact with other cells to induce a wide variety of biological effects (proliferation, apoptosis, angiogenesis, coagulation etc.). By comparing the genomic and proteomic networks of interacting and noninteracting cells, and overlaying these data with disease/mutation and pharmacological data, an opportunity arises for a much deeper understanding of the cell biological of the vascular system. The work described by Dittrich et al is certainly a positive step in that direction.

Disclosures

None.

References


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