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Given that the extremely elaborated and dynamic functions performed by the nervous system require the close synchronization of brain cells, complex organisms have developed different mechanisms of intercellular communication. At this regard, paracrine signaling between neighboring cells is currently recognized as one of the most widely distributed mechanisms of synchronization in the brain parenchyma. In mammals, paracrine signaling is in part mediated by single membrane channels formed by connexins (connexons/hemichannels) or pannexins (pannexons), which are two different membrane protein families composed of about 20 and 3 members, respectively. Single membrane channels formed by these proteins serve as aqueous pores permeable to ions and small molecules, allowing the diffusional exchange between the intra- and extracellular milieu. Thus, connexin hemichannels and pannexons permit the release of significant quantities of autocrine/paracrine signaling molecules (e.g., ATP, glutamate, NAD+, adenosine and PGE2) into the extracellular milieu, as well as the uptake of small molecules. An increasing body of evidence has revealed that connexin hemichannels and pannexons play a crucial role in a plethora of brain processes including blood flow regulation, Ca2+ wave propagation, memory consolidation, glucose sensing and cell migration and adhesion. Considering the multiple cell signaling functions of these channels, their dysregulation is proposed not only as potential

pathological biomarker, but it has been implicated in the pathogenesis and progression of diverse brain diseases (e.g., meningitis, Alzheimer's disease and stroke). The aim of this Research Topic is to gather a collection of original research articles, method, protocols, short communications, opinions, perspectives, as well as review articles, providing the latest progress and insights in the field of connexin hemichannels and pannexons in the nervous system. Within this volume we plan to cover from basic research including channel structure, regulation, pharmacology and trafficking; to different biological functions in the physiology (behavior, plasticity, neurogenesis, blood flow control, neuron-glia crosstalk, cell migration and differentiation) as well as in the pathophysiology (neuroinflammation, mutation-related diseases, glial dysfunction and neurodegeneration) of the nervous system. We hope that this collection of articles will serve to understand how the signaling of connexin hemichannels and pannexons influences both normal and pathological brain function.