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VENICE ASIAGO 2016

DATE: 29th August 2016

TIME: 9:00 - 12:00

LOCATION: Osservatorio Astronomico di Asiago, via dell'Osservatorio, 8; Asiago, Vicenza

Biochemistry and Biophysics of communication between cells

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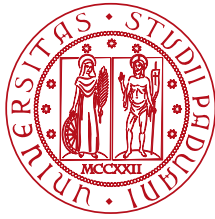
ABSTRACT

Connexin-made channels are essential and widespread constituents of the cell-cell communication pathways that enable the direct exchange of nutrients and signaling molecules between adjacent cells [1](#) or between cell cytoplasm and the extracellular medium [2, 3](#). Channel constituents are structurally homogeneous plasma membrane proteins encoded by twenty one connexin genes in the human genome [4](#).

Connexin proteins share the same topology, which comprises four transmembrane domains (TM1–TM4) connected by two extracellular loops (EC1 and EC2) and a cytoplasmic loop (CL), while the N- and C-termini (NT, CT) of the protein extend into the cytoplasm of the cell [5](#). Connexins are post-translationally oligomerized to form hexameric assemblies, known as connexons or hemichannels which are then trafficked to the plasma membrane.

Typically, connexons from one cell seek to partner and dock with connexons from adjacent cells to form an intercellular (gap junction) channel [1](#). These channels are characterized by an aqueous pore with a diameter typically > 1 nm [5, 6](#) and are permeable to all current-carrying anions and cations and low molecular weight molecules as well as some of the more important second messengers and paracrine factors involved in cell signaling [7, 8](#). Unpaired connexin hemichannels in the cell plasma membrane lack ion selectivity and mediate autocrine/paracrine signaling by the release or uptake of small molecules which are critical for cell-cell communication and the regulation of the key inflammatory responses [3, 9](#).

Mutations leading to changes in properties, regulation or expression of connexin-made channels have been implicated in a variety of human diseases that can affect nearly every human organ [10](#). In particular, mutations in GJB2 (MIM# 121011), the gene that encodes human connexin 26 (hCx26, where 26 indicated the molecular weight of the protein in kDa), are directly responsible for congenital sensorineural hearing loss; one of the most prevalent inherited diseases in the world [11](#). Most current pharmacological agents for connexin and pannexin inhibition are notoriously nonspecific, making it difficult to consider them in therapeutic designs. Therefore there is an urgent need for more selective connexin inhibitors and activators with defined mechanisms of action.



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