

Larsen W J. Structural diversity of gap junctions. A review.

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The structural diversity of gap junctions summarized in this review raised functional questions that seem to be particularly pertinent in the light of recent molecular studies of gap junction proteins. A variety of novel findings support the idea that gap junctions are highly dynamic structures. In addition, the cloning of cDNAs for at least two gap junction proteins and immunochemical data confirm the suggestion that gap junctions may be a related family of organelles rather than a single molecular species of structure. [The SCI® indicates that this paper has been cited in over 160 publications.]

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By the early 1970s it had become likely that the gap junction, one of many types of cell-to-cell membrane specializations discovered by then, was the structure that the function of intercellular communication was looking for. One widely accepted postulate of the field that developed as a consequence of this realization, however, was the idea that there was only one fundamental kind of gap junction, distributed from the most primitive coelenterates to man, that functioned as a relatively nonselective conduit permitting the passive cell-to-cell diffusion of small molecules.

Twenty years after the discovery of the gap junction, this idea continues to pervade most biology and basic cell-biology textbooks. In addition, little was known in 1977 regarding gap junction turnover, and the most typically discussed mechanism of functional modulation involved the physiological gating of gap junction pores. By the mid-1970s, however, freeze-fracture images indicated that the supramo-

lecular and topological organization of these seemingly simple organelles was quite variable from organism to organism and from tissue to tissue. It seemed to me at the time that an objective exploration of such structural diversity might provide clues to the possible functional bases for these differences, and so these were the issues I explored in my review.

I believe that this simple comparative approach contributed to the idea, discussed by only a few investigators in the field, that gap junctions were highly dynamic organelles. Recent biochemical work has confirmed this suggestion by demonstrating that gap junction proteins in liver have half-lives on the order of a few hours, which is considerably shorter than those of most other liver proteins.<sup>1,2</sup> A number of laboratories have also worked out many of the mechanistic details that underlie the synthesis, growth, structural differentiation, and degradation of gap junctions in a variety of tissues, and there is now significant interest in the possibility that functional modulation may also occur through gap junction turnover as well.<sup>3</sup>

This review, however, also provided support for the provocative notion, now gaining wide respectability, that "the" gap junction could be a family of structurally related organelles that might carry out diverse functions in different cells. Indeed, this suggestion has recently been supported and extended by exciting new information based on the cloning of cDNAs encoding gap junction proteins.<sup>4-6</sup> These data now demonstrate that a family of gap junction proteins exists, quite homologous at their amino ends and transmembrane regions but differing radically at the carboxy terminus. These novel data also show that these different proteins have somewhat different tissue distributions.

The ultimate number of gap junction proteins and the fundamental functional principles underlying their distribution remain to be determined. It is clear, however, that continuing molecular analysis will quickly provide more detailed data that address and, it is to be hoped, answer questions and observations discussed in my manuscript a decade ago.

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