Organization of receptors, ion channels and transporters along the neuronal surface

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Biological membranes are composed of two sheets of phospholipids with embedded integral and peripheral proteins, acting not only as a boundary of living cells but also as an interface among cells and their organella. Among integral proteins, molecular cloning has revealed over 200 genes encoding neurotransmitter receptors, ion channels and transporters in mammals, making them the most diverse subset of plasma membrane proteins. The precise location of neurotransmitter receptors, ion channels and transporters along the dendro-somato-axonic surface of the neurons, as well as at intracellular sites, is an important factor in determining its functional impact. However, they are not evenly distributed on the neuronal surface and depending on the protein subtype, are instead concentrated at different compartments. One factor necessary to understand their role in neuronal function is to unravel their specialized distribution and subcellular localization within a cell, and this can only be achieved by electron microscopy. The SDS-digested freeze-fracture replica labelling (SDS-FRL) technique is a powerful and cutting-edge approach for quantitative investigation of localization and the two-dimensional distribution of membrane molecules at a nano-scale spatial resolution. SDS-FRL was developed by combining a conventional freeze-fracture replica technique with an immunogold labelling approach for the molecules of interest. I will introduce a rationale, advantage and disadvantage of the SDS-FRL technique, in comparison with the conventional immunoelectron microscopy techniques, showing clear evidence that this highly sensitive approach provides comprehensive information on the organization of neurotransmitter receptors, ion channels and transporters in any given neuron and demonstrating their unique localization in a protein type-, subunit-, brain region-, cell type- and compartment-dependent-manner.
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