1. Record Nr. UNINA9910557404603321

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Titolo	The Tight Junction and Its Proteins : More Than Just a Barrier
Pubbl/distr/stampa	Basel, Switzerland, : MDPI - Multidisciplinary Digital Publishing Institute, 2020
Descrizione fisica	1 electronic resource (432 p.)
Soggetti	Medicine
Lingua di pubblicazione	Inglese
Formato	Materiale a stampa
Livello bibliografico	Monografia
Sommario/riassunto	For a long time, the tight junction (TJ) was known to form and regulate the paracellular barrier between epithelia and endothelial cell sheets. Starting shortly after the discovery of the proteins forming the TJ—mainly the two families of claudins and TAMPs—several other functions have been discovered, a striking one being the surprising finding that some claudins form paracellular channels for small ions and/or water. This Special Issue includes 43 articles covering numerous dedicated topics including pathogens affecting the TJ barrier, TJ regulation via immune cells, the TJ as a therapeutic target, TJ and cell polarity, function and regulation by proteins of the tricellular TJ, TJ as a regulator of cellular processes, organ- and tissue-specific functions, TJ as sensors and reacting to environmental conditions, and last but not least, TJ proteins and cancer.