Cells within the vast majority of human tissues communicate directly through clustered arrays of intercellular channels called gap junctions. Gene ablation studies in mouse models have revealed that these intercellular channels are necessary for a variety of organ functions and some of these genes are essential for survival. Molecular genetics has uncovered that germ line mutations in nearly half of the genes that encode the 21 member connexin family of gap junction proteins are linked to one or more human diseases. Frequently, these mutations are autosomal recessive while in other cases autosomal dominant mutations manifest as disease. Given the broad and overlapping distribution of connexins in a wide arrangement of tissues it is hard to predict where connexin-linked diseases will clinically manifest. For instance, the most prevalent connexin in the human body is connexin43 (Cx43), yet autosomal dominant mutations in the GJA1 gene that encodes Cx43 exhibit modest developmental disorders resulting in a disease termed Oculodentodigital Dysplasia (ODDD). Autosomal recessive mutations in the gene encoding Cx26 result in moderate to severe sensorineural hearing loss, while autosomal dominant mutations produce hearing loss and a wide range of skin diseases that include palmoplantar keratoderma. A new family of functionally related genes, termed pannexins, encode proteins that appear to have a primary role in constructing single membrane channels and early data suggest that they have tumor suppressive properties. At present, it is not known if any mutations in pannexins are linked to disease.