Ouabain-resistant Ma104 cells rescue co-cultured sensitive MDCK cells through the expression of a laminin rich extracellular matrix

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Canine kidney epithelial MDCK cells are sensitive to ouabain because, when incubated with this drug at concentrations of 250 nM or higher, it binds to its receptor, the Na+/K+-ATPase, and induces cell detachment from their neighbors and the substrate, in a process that requires the activation of the Src-MAPK-STAT3 signaling pathway. On the other hand, monkey kidney epithelial Ma104 cells are resistant to ouabain and do not detach when cultured in the same conditions. When both cell lines are co-cultured in media with ouabain, 50% of ouabain-sensitive MDCK cells remain attached, indicating that resistant cells "rescue" a significant proportion of the sensitive cells. Here, we investigated how Ma104 cells resist ouabain and confer ouabain resistance to sensitive MDCK cells in co-culture. In Ma104, ouabain activates the Src-MAPK-STAT3 signaling pathway with different kinetics than on MDCK cells. Ma104 cells express more extensive and abundant focal contacts than MDCK cells. The extracellular matrix of Ma104 cells is more abundant and enriched in laminin-β1 than the one of MDCK cells. When cultured on a laminin-rich extracellular matrix, these cells acquire ouabain resistance. These results indicate that ouabain-resistant cell adhesion depends, in part, on the expression of a laminin-rich extracellular matrix.