Verhandlungen der Anatomischen Gesellschaft,
97. Versammlung

Function of Rho protein in the process of trophoblast adhesion – in vitro studies on signalling mechanisms in human uterine epithelial RL95-2 cells

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Embryo implantation is initiated by adhesion of the trophoblast cells to the epithelial lining of the endometrium. In a model system mimicking basic cell biological processes involved here, human trophoblast-like JAR cells (JAR) are allowed to attach to and interact with a monolayer of human uterine epithelial RL95-2 cells (RL). As described previously molecular mechanisms important for JAR binding include Ca^{2+} signaling elicited in RL upon contact with JAR and this is dependent on apically localized integrins linked to the actin cytoskeleton. In the present communication we demonstrate that the RhoA pathway of RL is a link in this chain of events that lead to JAR adhesion. In particular, we explored the expression of RhoA by immunoblot analysis and fluorescence confocal microscopy, and correlated this with the expression and distribution of actin within cell-cell adhesion sites. Adhesion sites were found to show a large portion of RhoA located at the plasma membrane and high amounts of actin fibers in the plane of contact. Adhesiveness of RL for JAR spheroids was determined using a centrifugal force-based adhesion assay. In order to determine whether the Rho family plays a role in JAR binding, we treated RL with Clostridium difficile Toxin A (TcdA: 100 ng/ml for 24h) which ADP-ribosylates RhoA. The inactivation of RhoA was found to correlate with a reduction of JAR adhesion (52.9%). Additionally, a correlated reduction of adhesion-dependent Ca^{2+} influx (51.3%) was found. These data show that the RhoA pathway in RL plays a role for JAR binding; by extrapolation, the data suggest that RhoA might be an important element in the adhesion cascade during the embryo implantation.

Annals of Anatomy 184 (Suppl): 172-173, 2002