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Therapeutic Use of microRNA-200c to Treat HEY Ovarian Cancer

MicroRNAs (miRNAs) are known to play a large role in gene regulation. In particular, miR-200c is highly expressed in normal epithelial cells but not in breast, uterine, and ovarian cancer cells. When miR-200c is restored to aggressive ovarian cancer cells (HEY), the cells' characteristics change: as observed last year, HEY cells respond better to paclitaxel, a chemotherapeutic drug and migrate more slowly. Therefore, miR-200c is also hypothesized to affect HEY cell adhesion. Since 200c cells behave similarly to epithelial cells, they should not adhere as strongly as cancer cells. Adhesion assays were conducted, and the results for Collagen IV, Fibronectin, and Vitronectin support the hypothesis. Class3-beta-tubulin (TUBB3) is inappropriately expressed in certain chemotherapy-resistant cancers, so to determine the mechanism responsible for increasing sensitivity to paclitaxel, HEY cells were stably transfected with miR-200c and an expression vector encoding TUBB3 without the 3'UTR to which miR-200c binds. Empty vector (EV) transfected cells were the negative control. TUBB3 cells were hypothesized to be less chemosensitive since the over-expressioning TUBB3 without 3'UTR would reduce miR-200c's ability to target TUBB3 and restore HEY cells' chemosensitivity. Colonogenic assays assessed HEY cells' response to paclitaxel by quantifying surviving colonies, and the results also support the hypothesis. 30% of EV cells died when treated with 4 nM of paclitaxel, compared to 13.5% of TUBB3 cells. However, with only three successive trials, definitive conclusions cannot be drawn, and more experimentation is being done. Understanding how miR-200c works will help us determine the most efficient way to treat ovarian cancer.