Tiny protein provokes healthy bonding between cells

November 25 2008

In human relationships, a certain "spark" often governs whether we prefer one person to another, and critical first impressions can occur within seconds. A team lead by Johns Hopkins researchers has found that cell-to-cell "friendships" operate in much the same way and that dysfunctional bonding is linked to the spread of cancer.

The research was published in the Nov. 18 early online edition of the *Proceedings of the National Academies of Sciences* and appears in the journal's Nov. 25 print edition.

"Bonding between cells has important health implications," said the study's senior author, Denis Wirtz, a professor of chemical and biomolecular engineering in the Whiting School of Engineering at Johns Hopkins. "When cancer cells break free from their neighbors, they can spread the disease through the body. If we can learn more about this process, we may find new ways to keep cancer in check."

Toward that goal, Wirtz, who also is associate director of the Johns Hopkins Institute for NanoBioTechnology, led a multi-institution team that focused on alpha-catenin, a small protein that floats in the cytoplasm, the gel-like material that surrounds the nucleus inside a cell. Alpha-catenin allows cells to recognize neighboring cells as "friends" almost immediately, leading to the creation of many strong bonds that are hard to break. However, cancer cells, including those found in diffuse gastric cancer and lung cancer, possess dysfunctional alpha-catenin and form very weak bonds with their neighbors. This allows

them to break free from cell masses and spread cancer throughout the body.

To better understand these bonding characteristics, Wirtz and his colleagues used a technique called atomic force microscopy to study single cells with and without functioning alpha-catenin. This technique records tiny forces, measured in nanoNewtons, that cells exert upon one another.

Wirtz's team discovered that normal cells with properly functioning alpha-catenin formed bonds that were four times more stable than those without functional alpha-catenin, and these first bonds formed in less than 1 millisecond. The longer the cells remained in contact with one another, the more numerous and stronger these bonds became. The connections between these cells resembled those that occur with a popular type of fastener material. "This accelerated formation of additional bonds between neighboring cells was akin to the 'Velcro' effect," Wirtz said.

In contrast, cells without functional alpha-catenin formed weak bonds from the onset. Also, even as these cells remained in contact, bonding strengths continued to diminish. Wirtz suggested that if scientists could figure out a way to repair or replace the alpha-catenin dysfunction found in some cancer cells, it could lead to a therapy that thwarts the spread of cancer.

Link to the online journal article: www.pnas.org/content/early/200 … 783105.full.pdf+html

Source: Johns Hopkins University