Editorial Note

Stimulation and Repression of Cancer Development by Caveolae and Nitric Oxide

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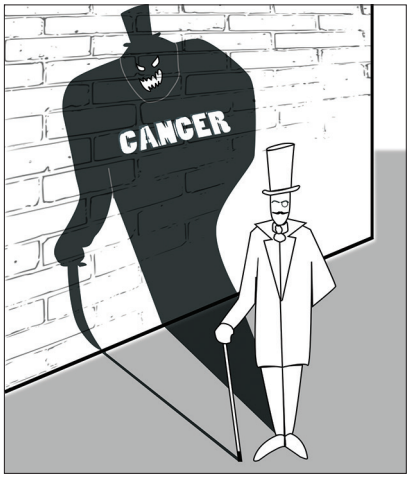
This issue of Biomedical Journal contains two reviews describing intracellular mediators that, depending on conditions, can either stimulate or repress tumors.

In the first review, Lamaze and Torrino propose a reconsideration of the involvement of caveolin-1 (Cav1) in cancer, whose role is still being debated.[1] Cav1 is a key component of small plasma membrane invaginations named caveolae, which can flatten out under mechanical stress to buffer an increase in membrane tension. For years, Cav1 has been described as either a pro- or an anti-tumorigenic agent depending on the stage of tumor development. In light of the new role of Cav1 and caveolae in sensing mechanical stress, Lamaze and Torrino hypothesize that mechanical forces encountered by cancer and stromal cells during tumor progression should drive a caveolae disassembly/reassembly cycle and therefore could control pro- or anti-tumoral signaling through release of free Cav1.

The second review by Monteiro *et al*.[2] describes in detail how nitric oxide (NO), a second messenger, that participates in a large number of cellular signaling pathways can also have pro- or anti-tumorigenic activities. The authors explain that oncogenic pathways involving epidermal growth factor receptor, Src, Ras or extracellular signal-regulated kinase/mitogen-activated protein kinase are activated when normal, or cancer cells are exposed to NO at low to intermediate concentrations. By modifying proteins (e.g. through tyrosine nitration, S-gluthathionylation, or S-nitrosylation), in this situation NO triggers cell proliferation and survival. Conversely, high intracellular NO concentrations lead to nitrosative stress conditions that favor cell death. Therefore, NO donors are now viewed as potential chemotherapeutic agents for cancer, although some selectivity issues remain to be solved.



These two examples illustrate perfectly how a small perturbation of cell signaling pathways can

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lead to tumor progression. A small glitch in an otherwise essential survival pathway opens the door for malignant transformation to sneak in much as Dr. Jekyll transforms himself into Mr. Hyde.

REFERENCES

1. Lamaze C, Torrino S. Caveolae and cancer: A new mechanical perspective. Biomed J 2015;38:367-79.
2. Monteiro HP, Costa PE, Reis AK, Stern A. Nitric oxide: Protein tyrosine phosphorylation and protein S-nitrosylation in cancer. Biomed J 2015;38:380-8.