

Anoikis Resistance: Survival of the Unplugged Cancer Cells

Shankargouda Patil¹, Roopa S Rao², Barnali Majumdar³

Contributors:

¹Associate Professor, Department of Oral Pathology & Microbiology, Faculty of Dental Sciences, MS Ramaiah University of Applied Sciences, Bengaluru, Karnataka, India; ²Professor and Head, Department of Oral Pathology & Microbiology, Faculty of Dental Sciences, MS Ramaiah University of Applied Sciences, Bengaluru, Karnataka, India; ³Postgraduate Student, Department of Oral Pathology & Microbiology, Faculty of Dental Sciences, MS Ramaiah University of Applied Sciences, Bengaluru, Karnataka, India.

How to cite the article:

Patil S, Rao RS, Majumdar B. Anoikis resistance: Survival of the unplugged cancer cells. J Int Oral Health 2015;7(10):i-ii.

Physiologically, the survival of the cells depends on their close mutual association with the matrix and their neighbor cells.¹ Due to certain factors, when this communication is lost; the cells undergo a unique type of apoptotic cell death, known as “anoikis.” It is derived from the Greek word meaning “loss of home or homelessness.”² Contrary to this phenomenon, the cancer cells show the ability to detach from the primary site and survive, migrate, and even flourish at a distant anatomic site.¹

The term anoikis was initially coined by Frisch and Ruoslathi.² It refers to the invocation of apoptosis in response to the detachment of the cell from the extra-cellular matrix.³ Under the physiological conditions, various mechanisms protect the cells from undergoing anoikis. In this context, the role of integrins has been highlighted. They aid in eliciting anti-apoptotic and pro-survival signals. Few molecules and pathways involved in this mechanism consist of focal adhesion kinases, Src kinases, phosphoinositide-3-OH kinases, mitogen-activated protein kinases, etc. Consequently, it is not unexpected to observe some of these molecules to be upregulated in the neoplastic cells. Other factors which inhibit anoikis, apart from cell-matrix adhesions, would be the cell-cell contacts maintained by the cadherins.⁴

Hence, ideally as the cell loses its attachment with the matrix or the adjacent cell, it should undergo anoikis. However, few exceptions are physiological cell migrations and spread of cancer cells. During physiologic migration of cells such as epithelial-mesenchymal transition and amoeboid motility, strong pro-survival signals are produced, or the cells glide through the matrix rather than complete detachment.⁴

Now, the query arises how the abnormal cancer cells escape anoikis and whether this phenomenon can be used to the advantage of cancer therapeutics. Concisely, anoikis resistance can be achieved via the death receptor (extrinsic) pathway, mitochondrial (intrinsic) pathway, by undergoing epithelial-mesenchymal transition, unregulated expression of growth receptors, altered cellular metabolism (Warburg effect), unbalance between redox reactions in the cellular signaling pathways and regulation of lipid raft localization.⁵

The central molecules which play the major role in the above-mentioned pathways can aid in targeted cancer therapies. For example, overexpression of FLICE-inhibitory protein (FLIP) antagonizes caspase-8 in the death receptor pathway, causing anoikis resistance in the tumor cells. Drugs like anisomycin can decrease the levels of FLIP, making the cells more sensitive to undergo anoikis. Other molecules which can be potential targets include Bim, BCL-2 modifying factor, cadherins and insulin-like growth factor-1, to mention a few.⁵

Escaping cell death, as well as ability to invade and survive in distant tissues is the two lethal properties of the cancerous cells. It seems anoikis resistance is yet another player, among several others in granting the malignant cells these features. Thus, with the increasing modern understanding of these molecular pathways and mechanisms of cancer development, the newer and specific drugs should offer an improved prognosis and survival of the cancer patients.

References

1. Liotta LA, Kohn E. Anoikis: Cancer and the homeless cell. *Nature* 2004;430(7003):973-4.
2. Sakamoto S, Kyprianou N. Targeting anoikis resistance in prostate cancer metastasis. *Mol Aspects Med* 2010;31(2):205-14.

3. Wazir U, Orakzai MM, Khanzada ZS, Jiang WG, Sharma AK, Kasem A, *et al.* The role of death-associated protein 3 in apoptosis, anoikis and human cancer. *Cancer Cell Int* 2015;15:39.
4. Paoli P, Giannoni E, Chiarugi P. Anoikis molecular pathways and its role in cancer progression. *Biochim Biophys Acta* 2013;1833(12):3481-98.
5. Kim YN, Koo KH, Sung JY, Yun UJ, Kim H. Anoikis resistance: An essential prerequisite for tumor metastasis. *Int J Cell Biol* 2012;2012:306879.