Spotlight

By M.O.

Tumor Control from Without

Martinkova *et al*.
10.1002/ijc.25187 (Resolve a DOI—http://dx.doi.org)

A network of transmembrane glycoprotein receptors anchors cells to the extracellular matrix and is critical for communicating extracellular cues to the cell and *vice versa*. The heterodimeric receptors are known as integrins and are composed of one alpha and one beta subunit. Different combinations of single alpha and beta subunits form at least 22 different receptors that possess distinct and often overlapping specificities for proteins in the extracellular matrix. While the vital function of integrins in cell motility and differentiation is well studied, the role of individual integrins in cancer biology remains ill-defined.

Martinkova and colleagues study drug-like antagonists of the alpha5beta1 integrin, specifically their effects on glioblastoma cell growth and survival in combination with standard chemotherapeutic drugs. Glioblastoma is a highly aggressive brain tumor notoriously resistant to chemotherapy. Evidence that alpha5beta1 integrins, receptors for fibronectin, may play a role in glioblastoma biology comes from studies showing that mRNAs of the individual subunits are upregulated in glioblastoma biopsies.

The authors show that the antagonists synergize with chemotherapeutic drugs to efficiently induce apoptosis in glioblastoma cell lines. This occurs through the inhibition of chemotherapy-induced senescence and involves the transcription factor p53 and its downstream target, the cyclin-dependent kinase inhibitor p21. Transcription of p21, which in glioblastoma cells is upregulated in response to chemotherapy, is suppressed when the antagonists are added to the treatment. These findings have direct implications for the clinical management of glioblastoma patients and point to an interesting new link between alpha5beta1 integrins and the p53 transcriptional network.