mTOR Targeting for Cancer Treatment

Madrid, November 16th, 2001 - The Journal of Clinical Oncology publishes in this month’s issue of “Understanding the Pathway” a paper by CNIO investigator Manuel Hidalgo, commenting on the role of mTOR as a cancer target and the strategies used to inhibit its function.

The mammalian protein mTOR is involved in the control of cell growth, proliferation and metabolism. During the last decade, a series of non-allosteric inhibitors of mTOR collectively named as Rapalogs have been developed for cancer treatment. Two of these drugs, temsirolimus and everolimus, have been approved to treat several patients with lymphoma, kidney cancer and neuroendocrine tumours. However, there are still important issues regarding the clinical application of these drugs. This is for example the case of brain tumours, where in spite of the high levels of mTOR activity, these cancers do not respond to the drugs. There are several explanations to this observation. One of them, which has been well-documented in preclinical and clinical studies, is that blockade of mTOR results in the activation of the AKT oncogene through a compensatory feedback mechanism. This and other observations have spurred a variety of strategies aimed at improving the therapeutic applications of inhibiting mTOR. On one end, there are a large number of clinical trials analysing combinations of mTOR with other targeted agents. However, despite the high scientific interest, toxicity issues may hinder the clinical development of these combinations. Alternatively, new drugs against mTOR or targeting both mTOR and its related protein, PI3K, are being developed. The advantage of using these agents is that they may indeed prevent the compensatory mechanism that activates AKT.

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