

Letter to the Editor

Targeting the RB pathway for cancer therapy: peptide mimetic foundations and promise

To the Editor:

In a recent survey in this Journal [1], Goldblatt and Lee discussed several relevant aspects of current translational research in cancer medicine. In addition to the coverage of conventional (chemo/radio)therapy and oncoprotein targets [1], we think that a review of this scope should have also touched, through a few representative examples, upon the vast range of antineoplastic retinoblastoma tumor suppressor (RB) pathway peptides developed over the past two decades. In this context, it is noteworthy that various investigators were able to reproduce the function of major tumor suppressor proteins of the RB pathway by much smaller synthetic peptides derived from these proteins. Accordingly, p21 [2], p16 [3] and RB [4] peptides were designed, synthesized and successfully tested against various human cancer cells, thus underscoring their candidacy as future anticancer drugs.

It is also important to point out that these efforts were the first of their kind to show that tumor suppressor pathways can be mimicked, or modified, by direct application of synthetic compounds. Later work using a similar approach paved the way for the development of the Nutlin series of compounds that target the p53 pathway. The industrial interest that was given these studies clearly shows how crucial these pioneering studies were.

We are therefore convinced that the development of these peptides ought to be intensified as, through further efforts, they might, as a single or combined [5] regimen, reward the arduous, yet worthwhile translation of natural tumor suppressors into their miniaturized artificial replicas by ultimately yielding those long-sought pharmacological agents with high potential to

fully replace conventional chemotherapy by virtue of a superior therapeutic index.

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