Origination of the concept of targeted, anti-evolutionary cancer therapy and identification of potential molecular targets for such therapy against clear cell renal cell carcinoma

Abstract

In contrast to organismal evolution, human cancers are subjected to similar initial conditions and follow a limited range of possible evolutionary trajectories. Until now, the predictable patterns of how cancer progresses have not been utilized for therapeutic benefits.

Evolutionary trajectories of clear cell renal cell carcinoma (ccRCC) have been recently described. I proposed strategies to take advantage of the evolving nature of these tumors for patients' benefit.

One of these strategies is to modulate tumor's genomic instability. In search for the best candidates for molecular targeting, I identified two proteins, TRIP13 and KIF11, and explored the relationships between their expressions and clinical course of ccRCC using the tissue microarrays (TMAs).

The TMAs contained specimens from 90 patients followed up for 7 years. All the tumor samples were evaluated for TRIP13 and KIF11 expression using immunohistochemistry and the H-score method. The overall survival (OS) was analyzed using the Kaplan-Meier method and log-rank statistics. Univariate and multivariate analyses were conducted using Cox proportional hazard models.

Cytoplasmic expressions of TRIP13 and KIF11 in ccRCC tissues were lower than those in adjacent controls ($P < 0.05$). I dichotomized the cytoplasmic expressions of these proteins to low and high expression using the tool Cutoff Finder. Both the elevated expressions of TRIP13 and KIF11 served as independent unfavorable prognostic indicators of survival in ccRCC ($P < 0.05$).

Elevated expressions of TRIP13 and KIF11 predict poor clinical outcome in ccRCC patients. Our results may serve as a starting point for translational research, in which the modulation of TRIP13 and KIF11 expressions could provide new therapeutic strategies for ccRCC.