Targeting tumour metabolism with chemopreventive molecules: AMPK as a molecular hub

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Angiogenesis is a crucial step in tumour growth and dissemination. Recently, increased attention has been addressed to the ability of different phytocompounds to prevent cancer by suppressing angiogenesis, strategy that we named "angioprevention". Adenosine-Monophosphate Activated Protein Kinase (AMPK) is an energy and metabolic sensor involved in several signalling pathways affecting a variety of cellular outputs, including cell survival, proliferation and metabolism. Several natural compounds exert their anti-tumour properties through AMPK. Here, we investigated whether known chemo-preventive, anti-angiogenic and angio-preventive compounds exert their action by targeting AMPK in tumour, endothelial cells and the tumour microenvironment.

We found that the biguanide Mertformin (METF), commonly employed in type-2-diabetes management, inhibits the formation of capillary-like networks by endothelial cells; this effect is partially dependent on the energy sensor adenosine-monophosphate-activated protein kinase (AMPK). Gene expression profiling of human umbilical vein endothelial cells revealed a modulation of several angiogenesis-associated genes and proteins by metformin [1]. In collaborative studies, we found that Aspirin and atenolol synergizes with Metformin in inducing apoptosis of triple negative and endocrine-sensitive BC cells, and in activating AMPK in BC and in white adipose tissue (WAT) progenitors known to cooperate to BC progression [2].

Finally, we demonstrated that the anti-angiogenic and angio-preventive activities of the hop derived flavonoid xanthohumol (XN) act through AMPK activation and its downstream signalling [4]. We are now evaluating the role of AMPK up- and down-stream signals.

Altogether, our data place AMPK as a relevant orchestrator of tumour metabolism and angiogenesis, representing a valid druggable target for chemopreventive and angiopreventive approaches.

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