

## Molecular biology of the traditional solutions of cancer

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In spite of the most recent advances in cancer therapeutics, cancer remains a killer disease. In last two -three decades cancer incidence has been increasing tremendously worldwide and hence has called an urgency in seeking new solutions to this problem. In the scenario of developing modern molecular bio-technologies, we considered to look into the traditional ways to fight cancer. In the traditional Indian medicine system (Ayurveda), Ashwagandha (*Withania somnifera*) is considered as a proud herb and often called ""Indian Ginseng"" or ""Queen of Ayurveda"". It has been assigned a variety of therapeutic potentials anti-inflammatory, antistress, antitumor, antioxidant, neuroprotective, immunomodulatory and forms a common ingredient of health supplements, tonics and Indian home remedies designed to promote health and quality of life. Although sheltered with experiences and long history of its use, there are only a limited laboratory studies and experimental evidence to its effects. In our efforts to characterize Ashwagandha activities and their molecular mechanisms, we initially prepared leaf extract of Ashwagandha (i-Extract) and assayed its anticancer activity in vitro using cultured normal and cancer cells. i-Extract showed selective cancer cell killing activity. We undertook a gene silencing approach to identify the cellular targets of i-Extract. Molecular analysis showed that i-Extract caused activation of p53 tumor suppressor pathway in cancer cells selectively. i-Extract was fractionated and its anticancer activity was assigned to its component, withanone by in vitro, in vivo and chemical analyses. Besides activation of p53 in cancer cells, i-Extract and i-Factor also inactivated telomerase activity in cancer cells. Most recently, we found that a major withanone protected the normal human fibroblasts against the toxicity caused by withaferin A. It increased the in vitro division potential of normal human cells that was mediated by decreased accumulation of molecular damage, down-regulation of a senescence specific  $\beta$ -gal activity and a senescence-marker protein, p21WAF-1, protection against oxidative damage and induction of proteasomal activity. To the best of our knowledge, we provide the first example of phytochemicals (i-Extract and i-Factor) that have both anti-cancer and anti-aging activities and point to the molecular link between aging and cancer.

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3. Widodo, et al. (2008) Selective killing of cancer cells by leaf extract of Ashwagandha: Components, activity and pathway analyses. *Cancer Lett.* 262: 37-47.
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