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Cancer Prevention Research

The Forefront of Prevention Science

May 2013 • Volume 6 • Number 5

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ABOUT THE COVER

Melanoma, the most aggressive form of skin cancer, accounts for 75% of skin cancer mortality. The activation of the signaling cascade comprising BRAF-NRAS-MEK1/2-ERK1/2 is an important trigger for melanoma survival, growth and proliferation. Several studies have demonstrated the chemopreventive and/or chemotherapeutic effects of silybin, a major bioactive component of milk thistle (*Silybum marianum*), against various cancers. Virtual screening revealed that silybin is a potent inhibitor of the BRAF-MEK-ERK-RSK2 signaling pathway. The direct binding of silybin with RSK2 (ribbon structure shown) and MEK1/2 (not shown) was generated using the Schrödinger Induced Fit docking program. Silybin was shown to significantly inhibit melanoma cell growth *in vitro* and *in vivo* through its direct binding with MEK1/2 and RSK2, resulting in the inhibition of their catalytic kinase activities and subsequent reduction in the activation of NF- κ B, AP-1 and STAT3—transcriptional regulators of a variety of proliferative genes in melanomas. See article by Lee and colleagues (beginning on page 455) for more information.



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Cancer Prev Res 2013;6:371-506.

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