

7<sup>th</sup> Global Summit on  
**Cancer Therapy**

October 05-07, 2015 Dubai, UAE

**Thymidylate synthase-dependent down-regulation of NF- $\kappa$ B is the pivotal signaling mechanism regulating curcumin-mediated chemo-sensitization of breast cancer cells to 5-FU**

**Haritha H Nair**

Rajiv Gandhi Centre for Biotechnology, India

Breast cancer is always a mystifying puzzle owing to the wide contrast in its responsiveness to treatments. Most of the currently available chemotherapeutics against breast cancer fail to confer the maximum clinical efficacy because of the adverse side effects and gradual development of chemo-resistance, which they induce by up-regulation of various survival signals and multi-drug resistance genes. Chemo-sensitization can be a choice that absolutely matches the need. Several phytochemicals has been reported to modulate multiple pathways involved in chemo-resistance when used in combination with conventional chemotherapeutics and are preferred over other compounds because of their pharmacological safety. Previous *in vitro* studies conducted in the lab have shown that a combination of 10  $\mu$ M curcumin and 10  $\mu$ M 5-Fluorouracil (5-FU) can bring down the amount of the chemotherapeutic needed for inducing apoptosis in breast cancer cells, independent of their receptor status. The study also found that curcumin down-regulates several survival signals, including Thymidylate Synthase (TS), the key enzyme for de novo synthesis of DNA whose over-expression in cancer cells leads to 5-FU chemo-resistance. We also observed that curcumin is capable of down regulating several survival signals like Akt, MAPKs and NF- $\kappa$ B, which are found to be up-regulated by 5-FU when given alone. Moreover, curcumin induces apoptosis in breast cancer cells by regulating Bcl-2, Bcl-XL, survivin and caspases. However, the pivotal molecule which regulates the synergism was unclear. The present study was intended to identify the key regulatory molecule and the signaling events that regulate the synergism.

**Biography**

Haritha H Nair is currently pursuing her PhD under the guidance of Dr. Ruby John Anto in the Division of Cancer Research, Rajiv Gandhi Centre for Biotechnology, India. She has completed Masters in Biotechnology from Amrita School of Biotechnology, Kollam. Her topic of research is "Mechanistic evaluation and *in vivo* validation of synergistic combinations of curcumin and resveratrol with chemotherapeutics in breast cancer treatment". She is the first author of review article and co-authored in the paper.

[harithahnair@rgcb.res.in](mailto:harithahnair@rgcb.res.in)

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