Title of project: **Modulation of Nitric Oxide synthases and induction of apoptosis in hepatocellular carcinoma by fisetin** (UGC File No. 41-71/2012 (SR))

**PI:** Prof. S.K. Trigun, Deptt. Zoology, BHU, Varanasi-5; email: sktrigun@gmail.com

**Abstract**

This project aimed to investigate whether Fisetin (a natural flavonol, found in common fruits and vegetables) was able to modulate the tumor growth supportive biochemical adaptations. The profiles of inflammation-oxidative stress-apoptosis pathway vis a vis iNOS (inflammation triggering factor) & e-NO (neoangiogenic inducer) and cell growth promoting factors; PI3K signaling; Akt, PTEN, PDK, GSK3β & PCNA, were evaluated in AFB1 (a common HCC causing fungal intoxicant) induced HCC rat model.

As illustrated in a graphical chart, findings suggest that (1) AFB1 induced HCC pathogenesis implicates oxidative stress-inflammation-iNOs & e-NOS led Akt signaling cascade. However, Fisetin treatment could effectively attenuate all the tumor growth associated biochemical and molecular targets which underwent aberrant activation during tumorigenesis. This was consistent with normalization of HCC markers and enhancement in life span of the fisetin treated HCC rats.

![Schematic presentation: Putative mechanism proposed for how Fisetin inhibits HCC growth in vivo. Solid arrows show cell growth promoting cascade and empty arrows/lines show Fisetin effects.](image)

**Take home message:** The findings define cell growth signaling cascade as therapeutic targets of fisetin, a natural flavanol, in an in vivo HCC model and thereby advocate for (a) exploring translational feasibility of fisetin as an effective anticancer agent and (b) consumption of fisetin rich fruits and vegetables as tumor preventive regimen.