

## **KEY PATHWAYS AND EMERGING PLAYERS IN HUMAN MELANOMA DEVELOPMENT AND PROGRESSION**

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Melanoma is the most common form of skin cancer. Given its high mortality, the interest in the search of preventive measures is growing significantly. Hydrogen sulfide (H<sub>2</sub>S) is a gaseous signalling molecule that plays important roles in a variety of biological functions in health and disease (Paul & Snyder, 2015). Emerging data indicate that H<sub>2</sub>S is also involved in the regulation of tumor cell biology (Hellmich MR, Szabo C. 2015). However, the effects of H<sub>2</sub>S on cancer are controversial and still unclear. It has been shown that H<sub>2</sub>S induces DNA damage and alter cell cycle in various mammalian cells. Endogenously produced or exogenously released H<sub>2</sub>S has a role in the accumulation or proliferation of cells and further may provide the fundamentals for development of a novel therapeutic approach in conditions associated with uncontrolled cell growth (Baskar and Bian, 2011). However, the potential biological and clinical significance of H<sub>2</sub>S are subject of intense debate in recent years and despite considerable progress in our understanding about H<sub>2</sub>S, much still needs to be learned about their production at the site of tissue injury and its downstream signalling pathways on cell growth. It is also important to emphasize that in the recent literature different roles have been attributed in several types of cancer to CBS-derived H<sub>2</sub>S and to CSE-derived H<sub>2</sub>S. Moreover many of the biological responses to H<sub>2</sub>S follow a biphasic dose-response: while low concentrations of H<sub>2</sub>S are responsible of physiological and cytoprotective effects, high concentrations result cytotoxic (Szabo, 2016). We have recently demonstrated that the metabolic pathway l-cysteine/CSE/H<sub>2</sub>S is involved in human melanoma progression and that natural and synthetic H<sub>2</sub>S releasing agents display anti-tumoral effect (Panza et al., 2015). Our results establish H<sub>2</sub>S-donors as new potential agents in the treatment of human metastatic melanoma and represent a very promising strategy to improve the fight against cancer.

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