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Dr. Ka Bian is a Principal Investigator in Research and Development at the VA Palo Alto Health Care System (VAPAHCS). The Bian laboratory has discovered multiple roles of nitric oxide (NO), soluble guanylyl cyclase (sGC), and cyclic guanosine monophosphate (cGMP) in tumor biology, which made a paradigm shift of this key signaling pathway from the cardiovascular system to cancer biology and therapy.

NO participates in normal signaling (e.g., vasodilation and neurotransmission); however, NO has cytotoxic or proapoptotic effects when produced at high concentrations by inducible nitric oxide synthase (iNOS or NOS-2). In addition, the levels of the cGMP-dependent (the NO/sGC/cGMP pathway) and cGMP-independent (the NO redox pathway) components vary between various tissues and cell types. Frequent deregulation of sGC expression at the levels of transcription, splicing, mRNA stability, and protein stability have been investigated. Solid tumors include two compartments, the parenchyma (neoplastic cells) and stroma (nonmalignant supporting tissues including connective tissue, blood vessels, and inflammatory cells), and biological properties and signaling pathways influenced by NO are different in these compartments. Thus, specific features of the NO/sGC/cGMP signaling pathway should be further characterized in the tumor and surrounding tissues. Our previous study provided evidence for two possible roles of NO/cGMP signaling in malignant tumors. First, NOS-2 expression and NO overproduction contribute to the formation of an inflammatory cancer microenvironment, which promotes tumor cell proliferation. Second, a deficiency in sGC/cGMP signaling diminishes the role of these molecules as antagonists of cancer cell growth.

Recently, Dr. Bian's study revealed that sGCβ1 subunit alone can migrate into the nucleus, thus impacting malignant cellular signaling which including the promotion of nuclear accumulation of p53, a marked reduction in CDK6, and significant inhibition of integrin α6. These anticancer targets of sGCβ1 have been validated by various clinical studies and by the development of therapeutic strategies for cancer treatment. sGCβ1-based cancer therapy is characterized by boosting normal endogenous signaling and promoting differentiation of the tumor cells, which may transform the treatment by shifting the paradigm from the killing of cancer cells to differentiation-induced transformation of cancer cells.

For additional information, to participate in research, or to support our research contact Dr. Ka Bian at ka.bian@va.gov.