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Biogenic Selenium Nanoparticles Produced by the Probiotic *L. casei* and Selenium Nanoparticles-enriched *L. casei* as Bioactive Dietary Compounds Against Colon Cancer

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ABSTRACT

Selenium (Se) is an essential trace element that exerts multiple and impressive health-promoting effects including immunoregulatory [1], anticancer [2] and chemopreventive [3] activities. There is though, a very narrow window between the beneficial/therapeutic dose of Se and the dose that exerts toxicity [4]. Nanomaterials, due to the enhanced role of surface interactions and weak intermolecular forces, display different physicochemical properties compared to bulk materials [4]. As such, Se nanoparticles (SeNps) possess distinct physicochemical characteristics compared to other selenium forms. Noteworthy, SeNps are less toxic and have better bioavailability [5].

Herein, we achieved green synthesis of SeNps utilizing the probiotic *Lactobacillus casei* ATCC 393 (LC), a bacterial strain previously shown to exert antitumor effects against colon cancer [6,7]. We studied the potential of LC-derived SeNps as well as SeNps-enriched LC as bioactive compounds against colon cancer employing *in vitro* and *in vivo* pre-clinical colon cancer models. SeNps exerted cancer-specific growth inhibitory activity and increased immunogenicity in colon cancer cells. Noteworthy, oral administration of SeNps or SeNps-enriched LC, induced a significant 50% or 75% respectively, inhibition in tumor volume compared to control animals, in the CT26 syngeneic BALB/c colon cancer model. The observed *in vivo* tumor growth inhibition was accompanied by higher levels of serum IFNγ, a critical regulator of innate and adaptive immunity [8], and IL-12, a cytokine with a protective role against colon cancer [9]. Moreover, SeNps, downregulated the expression of cytochrome c in HT29 human colon cancer cells -an effect that has been linked with increased immunogenicity- and induced the translocation of calreticulin to the cell surface, a process associated with immunogenic cell death.

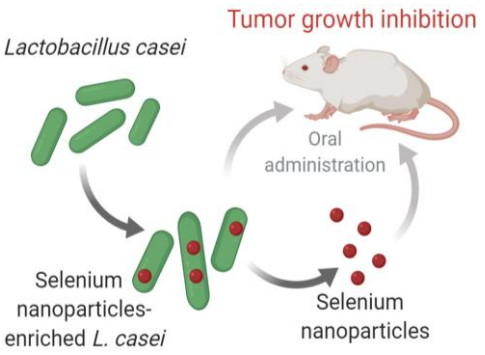

Figure 1. Biogenic selenium nanoparticles synthesized by the probiotic *Lactobacillus casei* inhibit colon cancer cell growth *in vitro* and *in vivo* when administered orally in mice.

We provide evidence that SeNps produced by LC and SeNps-enriched LC could be good candidates for the development of oral formulations or dietary supplements for the chemoprevention of colon cancer. Our results demonstrate the strong potential of nanoparticles-enriched probiotics for cancer prevention while highlighting the exciting prospects of their exploitation in pharmaceutical and food industries.

Keywords: selenium nanoparticles, biogenic, *Lactobacillus casei*, colon cancer

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