1. **An immunomodulatory gallotanin-rich fraction from *Caesalpinia spinosa* enhances the therapeutic effect of anti-PD-L1 in melanoma**

**Global Integrative Oncology: Use in Cancer Treatment & Patient Management**

**Background:** The PD-1/PD-L1 pathway plays a role in inhibiting immune response. Therapeutic antibodies aimed at blocking the PD-1/PD-L1 interaction have entered clinical development and have been approved for a variety of cancers. However, the clinical benefits are only present in a restricted group of patients. Currently, the research in combined therapies, which allows for a greater response, are strongly encouraging. We previously characterized a polyphenol-rich extract from *Caesalpinia spinosa* (P2Et) with anti-tumor activity in both melanoma and breast carcinoma, as well as immunomodulatory activity. We hypothesize that the combined treatment with P2Et and anti-PD-L1 can improve the antitumor response through an additive antitumor effect.

**Aim:** We investigated the antitumor and immunomodulatory activity of P2Et and anti-PD-L1 combined therapy in B16-F10 melanoma and 4T1 breast carcinoma.

**Methodology:** We analyzed tumor growth*,* hematologic parameters, T cell counts, cytokine expression, and T cell cytotoxicity.

**Results:** In the melanoma model, combined P2Et and anti-PD-L1 therapy has the following effects: decrease in tumor size; increase in the number of activated CD4+ and CD8+ T cells; decrease in the number of suppressor myeloid cells; increase in PD-L1 expression; decrease in the frequency of CD8+ T cell expressing PD-1; improvement in the cytotoxic activity of T cells; and increase in the IFNγ secretion. In the breast cancer model, P2Et and PD-L1 alone or in combination show antitumor effect with no clear additive effect.

**Conclusions:** This study shows that combined therapy of P2Et and anti-PD-L1 can improve antitumor response in a melanoma model by activating the immune response and neutralizing immunosuppressive mechanisms.

*Paola Lasso1, Alejandra Gomez-Cadena1,2, Claudia Urueña1, Alena Donda3, Amaia Martinez Usatorre4, Pedro Romero3, Alfonso Barreto1,Susana Fiorentino1\**

*1 Grupo de Inmunobiología y Biología Celular, Pontificia Universidad Javeriana, Bogotá, Colombia.*

*2 University of Geneva, Department of Pathology and Immunology, Geneva, Switzerland.*

*3 University of Lausanne, Department of Fundamental Oncology, Lausanne, Switzerland.*

*4 Swiss Federal Institute of Technology Swiss Institute for Experimental Cancer Research, Lausanne, Switzerland*