

Title	Systems biology strategy to regulate the proinflammatory response and enhance the cancer cell death
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Abstract	Tumor or cancer immunology is a new and fast growing field where the interactions of the inherent immune system with malignant cancers have shown the suppression of disease progression. In this field, systems biology approach is required to understand and control the cellular response, since cellular behaviors are highly dynamic, complex and well orchestrated. This thesis describes the current understanding of the systems biology approach and addresses the connectivity between immunology and systems biology. The main aims of this research are i) to regulate the proinflammatory response in Tumor necrosis factor (TNF) signaling pathway and ii) to understand the resistance mechanisms for cancer treatment in TNF related apoptosis inducing ligand (TRAIL) signaling pathway. Therefore dynamical computational models were developed using the well-established perturbation response approach, and analyzed the dynamics of key signaling molecules and gene expressions were analyzed. Using this systems biology approach, a key molecule was identified to effectively regulate, but not abolish, the proinflammatory response in TNF signaling and we also found a target to enhance cell death in TRAIL resistant cancer cells. This work shows systems biology approach integrating computational approaches and wet bench experiments shed light on the drug development for the regulation of the immune-mediated diseases.
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# Systems biology strategy to regulate the proinflammatory response and enhance the cancer cell death

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## Abstract

Tumor or cancer immunology is a new and fast growing field where the interactions of the inherent immune system with malignant cancers have shown the suppression of disease progression. In this field, systems biology approach is required to understand and control the cellular response, since cellular behaviors are highly dynamic, complex and well orchestrated. This thesis describes the current understanding of the systems biology approach and addresses the connectivity between immunology and systems biology. The main aims of this research are i) to regulate the proinflammatory response in Tumor necrosis factor (TNF) signaling pathway and ii) to understand the resistance mechanisms for cancer treatment in TNF related apoptosis inducing ligand (TRAIL) signaling pathway. Therefore dynamical computational models were developed using the well-established perturbation response approach, and analyzed the dynamics of key signaling molecules and gene expressions were analyzed. Using this systems biology approach, a key molecule was identified to effectively regulate, but not abolish, the proinflammatory response in TNF signaling and we also found a target to enhance cell death in TRAIL resistant cancer cells. This work shows systems biology approach integrating computational approaches and wet bench experiments shed light on the drug development for the regulation of the immune-mediated diseases.

**Keywords:** TNF, TRAIL, Cell signaling, Computational model, Inflammation, Cancer, Apoptosis