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From neuromodulation to drug discovery and treatment

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Polymicrobial sepsis is a leading cause of death in the ICU characterized by detrimental systemic inflammatory response leading to multiple organ failure. We reported that electrical vagal stimulation controls systemic inflammation and prevents multiple organ failure in severe sepsis. We recently reported that transdermal neuronal stimulation attenuates the innate immune response to bacterial infection and prevents multiple organ failure during experimental sepsis. These effects were mediated by the induction of dopamine from the adrenal medulla. However, recent studies indicate that most of the septic patients have adrenal insufficiency and neuronal stimulation failed to control inflammation in adrenalectomized animals. Thus, transdermal neuronal stimulation will fail to induce dopamine and to control inflammation in these patients. Our pharmacological studies indicated that dopamine controls inflammation and improves survival in experimental sepsis by activating dopaminergic receptors type-1 (DR1). DR1-agonists such Fenoldopam was more efficient than Dopamine at inhibiting LPS-induced TNF production in macrophages and also inhibiting serum TNF levels in experimental endotoxemia. *In vivo*, DR1-agonists inhibit the production of inflammatory factors including TNF, IL1, IL6 and INF- γ even in adrenalectomized animals that mimic adrenal insufficiency in septic patients. These results indicate that pharmacological translation of neuromodulation can provide new insights for treating sepsis.

Biography

Ulloa L is a Professor of Surgery at New Jersey Medical School at Rutgers, The State University of New Jersey, USA. He has completed his Post-doctoral training at the Memorial Sloan Kettering Cancer Center, New York. He is an expert in neuro-immune modulation and its translational research for treating infectious and inflammatory disorders such as in sepsis. He has published more than 76 articles in prestigious peer-review journals and is currently serving as an Editorial Board Member of reputed journals.

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