EXTRACELLULAR HISTONES AS BIO MARKERS FOR PROGNOSIS AND TARGETS FOR THERAPY
Background

• Hyper-inflammatory responses can lead to a variety of diseases

• Extracellular histones are released in hyper-inflammatory conditions and are mediators contributing to disease progression

• Diseases include bacterial or fungal sepsis, traumatic hemorrhage, acute pancreatitis, acute respiratory distress syndrome, ischemia reperfusion injury, cardiovascular disease, autoimmune disease, chemotherapy toxicity, radiotherapy toxicity, cytokine therapy toxicity, or burn

• Thus, histones can be targeted pharmacologically by inhibitors, as well as used as biomarkers for prognosis of these diseases
Solution

**Problem**

Hyper-inflammation

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Release of histones

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Cytotoxic histones cause cellular dysfunction

organ failure and death

**OMRF’s Solution**

Generate histone peptide analogs and anti-histone antibodies to block histone toxicity as a therapeutic

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Develop immunoassays for diagnosis and prognosis
Data

Graph demonstrates cytotoxicity of an extracellular histone mixture and individual histones toward endothelial cells in culture
Data

Survival rates of mice injected intravenously with histones with or without a proteolytic enzyme of histones (APC)

Survival rates of mice injected intravenously with LPS plus an antibody to H4 or mouse IgG control antibody
Summary

- Esmon et al have discovered that histones play a major role in the pathogenesis of hyper-inflammatory diseases and conditions. Treatment with polyclonal or monoclonal anti-histone antibodies can protect against organ failure and death.

- Histones can be targeted pharmacologically by inhibitors, as well as used as biomarkers for prognosis of these diseases.
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