## The effect of titanium alloy and stainless steel implants on immunological responses by analysis of NF-κB/ p65, NF-κB1/p50 profiles and the Tregs

Sibel Akyol<sup>1,2</sup>, Murat Hanci<sup>3</sup>, Besim Ben-Nissan<sup>2</sup>

<sup>1</sup>Istanbul University Cerrahpasa, Cerrahpasa Medical Faculty, Department of Physiology, Istanbul, Turkey

<sup>2</sup>University of Technology Sydney, Faculty of Science, School of Life Sciences, Sydney, Australia

<sup>3</sup>Istanbul University Cerrahpasa, Cerrahpasa Medical Faculty, Department of Neurosurgery, Istanbul, Turkey

**Introduction:** A comprehensive understanding of the tissue-biomaterial interactions at a cellular level is required to explain the immune responses of numerous implant mediated complications and help to improve biomaterial design and use.

**Objectives:** To research the effect of titanium alloy and stainless steel implants on immunological responses in rats by analysis of NF- $\kappa$ B/ p65, NF- $\kappa$ B1/p50 profiles in the activation of inflammatory signaling pathways and the role of Tregs. To minimize the inflammatory response of host-formed bio-material implants is our main goal.

**Materials and Methods:** In this study, 39 Wistar albino male rats were divided into three groups with 13 rats each resulting in Group I (n: 13, sham), Group II (n: 13, Ti alloy rods), and Group III (n: 13, SS alloy rods). The NF- $\kappa$ B/ p65, NF- $\kappa$ B1/p50 and CD4+CD25+Foxp3+ (Tregs) in the blood were analyzed on days 7, 14 and 28 using ELISA and Flow cytometry.

**Results:** Tregs level were lower in the stainless steel (SS) alloy compared to the sham and Titanium (Ti) alloy. NF- $\kappa$ B/ p65 (RelA) levels in the SS alloy showed a significant increase on all days in comparison with the sham and Ti alloy. NF- $\kappa$ B1 (p50) in the SS alloy was a significant increase on the 14<sup>th</sup> and 28<sup>th</sup> day. When the Ti alloy was compared with the SS alloy, NF- $\kappa$ B/ p65 (RelA) and NF- $\kappa$ B1 (p50) levels were significantly lower levels.

**Conclusions:** Both the Ti alloy and SS alloy group implantation effects CD4+CD25+Treg cells in different ways. This work suggests that NF- $\kappa$ B/ p65, NF- $\kappa$ B1/p50 have excellent potential as a therapeutic target in the prevention of adverse reactions to metal, especially for controlling the inflammation after the implantation. In

this application target can be NF-kB and for this IKK molecule inhibitors can be used or it can be done by the stabilization of IkB proteins.

Keywords: Titanium alloy implants, stainless steel implants, immunological response, NF- $\kappa$ B/ p65, NF- $\kappa$ B1/p50, Tregs