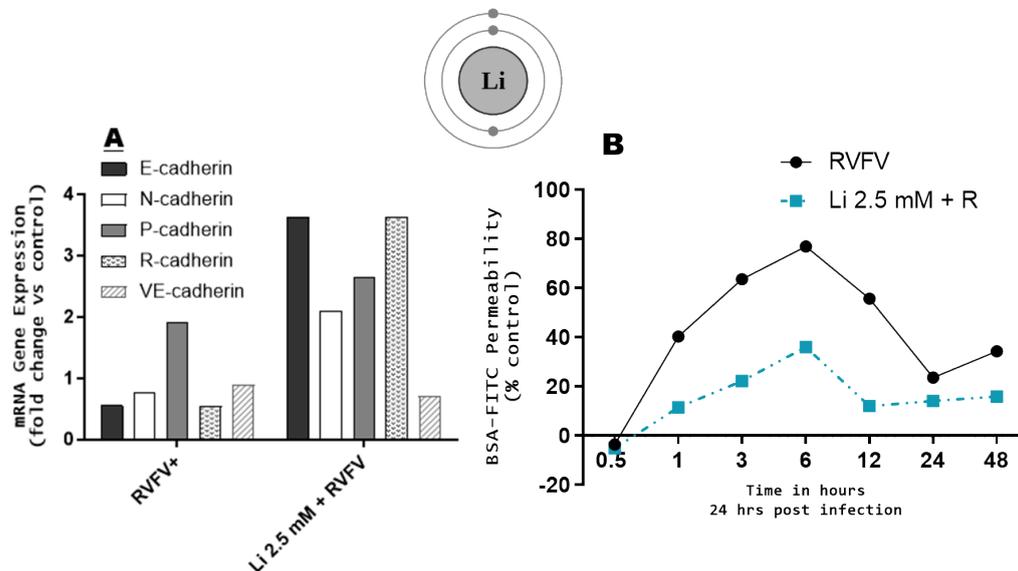


**Lithium preserves endothelial integrity by inhibiting rift valley fever virus-incuded inflammation in Raw 264.7 macrophages in anindirect co-culturing model system**

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**Figure 1: The effect of lithium pre-treated Raw 264.7 macrophage cells supernatant on adherence junction gene expression profiles[A] and integrity[B] of HUVEC cells monolayer.**

**Introduction:** Haemorrhagic fever, caused by Rift Valley fever virus (RVFV), is characterised by altered endothelial integrity from damaged endothelial cells that results in septic shock and multiple organs failure leading to death. The exact RVFV pathogenesis that leads to haemorrhagic fever remains poorly understood. Therefore, this study hypothesises that oxidative stress leads to endothelial leakage which culminates into haemorrhagic fever.

**Methodology:** The Huvec endothelial monolayer was used to represent the blood vessels integrity model and the xCelligence system together with the Transwell assay were used to measure endothelial integrity. The RT-PCR Profiler Array system was employed to examine expression of cell-to-cell junction-associated genes.

**Results:** Results from the xCelligence system showed that endothelial cells exposed to supernatants from RVFV-infected and lithium-treated Raw 264.7 cells displayed a cell integrity index of above 4.0 as compared to control cells. The transwell assay results showed that supernatants from lithium (1.25 and 2.5 mM)-treated RVFV-infected Raw 264.7 cells demonstrated protective properties compared to RVFV-inoculated Raw 264.7 cells not treated with lithium. Supernatants from lithium-treated cells upregulated expression of cytoplasmic molecules such as  $\alpha$  and  $\beta$ -catenins, talins, zyxins, as well as vinculins. Moreover, lithium was observed to express transmembrane molecules such as E-cadherin, P-cadherin, R-cadherin and N-cadherin. The expression of VE-cadherins was, however, observed to be lower compared to expression induced by supernatants from control RVFV-infected Raw 264.7 cells.

**Discussion:** The endothelial integrity observed in the permeability assays can be correlated with the expression of the molecules involved in keeping the cell to cell junction intact.

**Conclusion:** This study links the anti-inflammatory properties of lithium with preservation of endothelial integrity.

**Reference:**

Birukova AA, Shah AS, Tian Y, Gawlak G, Sarich N, Birukov KG (2016) Selective role of vinculin in contractile mechanisms of endothelial permeability. *Am J Respir Cell Mol Biol.* 55:476–486. **Key words.** Lithium, endothelial integrity, inflammation, RVFV