The Effect of ML 141 and Simvastatin on HUVEC/Fibronectin Binding

Komanapalli, Sarah

Invasive infection by the bacterium Staphylococcus aureus causes life-threatening diseases, including pneumonia and sepsis, a full-body inflammatory response. Currently, antibiotics such as penicillin, methicillin, and vancomycin are used to treat S. aureus infections. However, several cases of antibiotic resistant S. aureus have been reported, making infections more deadly and difficult to treat. This project demonstrates the effectiveness of the cholesterol-lowering drug simvastatin and the compound ML 141 as alternatives to antibiotics. S. aureus invades endothelial cells by binding to the extracellular protein fibronectin. Endothelial cells naturally engulf fibronectin; any S. aureus bound to the fibronectin is then brought into the cell. Previous studies have shown that patients taking statins are less susceptible to pneumonia and sepsis. This project sheds light on the molecular mechanism, showing that simvastatin inhibits the binding of fibronectin to human umbilical vein endothelial cells (HUVEC). The compound ML 141 was also shown to inhibit this interaction. In the experiment, one group of cells was exposed to dimethyl sulfoxide (control) and another group exposed to simvastatin in dimethyl sulfoxide. The number of cells that bound to fibronectin was counted using flow cytometry. The experiment was repeated using ML 141 instead of simvastatin. Fewer cells were counted in the samples treated with simvastatin or ML 141, indicating that simvastatin and ML 141 decrease binding of host cells to fibronectin. In this way, both simvastatin and ML 141 limit invasion. This experiment shows the potential for alternative methods of treatment not reliant on antibiotics.

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