

## **Quorum Sensing, Biofilm Formation, and NF- $\kappa$ B Inhibition by Plant Natural Compounds Derivatives**

The speaker: Yael Schlichter Kadosh, PhD student. Supervision: Prof. Ariel Kushmaro

The Environmental Biotechnology Laboratory, Department of Biotechnology Engineering, BGU.

Bacterial communication, termed Quorum Sensing (QS) is a promising target for virulence attenuation and treatment of bacterial infections. Several QS compounds have been proposed as possible therapeutics for such infections in recent years. Furthermore, since inflammation is regulated by several cellular factors including the transcription Nuclear Factor kappa B (NF- $\kappa$ B), which is found to be upregulated in many chronic inflammatory diseases induced by bacteria. This project aims to demonstrate our natural-based synthetic compounds' activities in inhibiting bacterial communication (QSI), bacterial virulence, and inflammation (via NF- $\kappa$ B) and to develop an active molecule for treatment against chronic bacterial infections. We screened 71 compounds, 4 of which are the original molecules and 67 derivatives originating from Coumapherine (CP), Piperlongumine (PL), Pterostilbene (PTS), and Curcumin (CU). In the screening, we found that out of all the tested compounds, PL-18 was most effective in inhibiting QS of *Pseudomonas aeruginosa*, and also inhibits secretion of virulence factors, and biofilm formation without being toxic to *P. aeruginosa*. PL-18 also efficiently inhibited NF- $\kappa$ B activation in two cell-lines, epithelial cells of the lung -A549 and Hodgkin lymphoma cells - L428. NF- $\kappa$ B inhibition is via upstream target to NF- $\kappa$ B, inhibition was in non-cytotoxic conditions. Taken together these results show that QS inhibition is a promising approach to prevent bacterial virulence by disturbing bacterial communication. Coupled with its ability to inhibit NF- $\kappa$ B induced inflammation, PL-18 presents a suitable candidate as a potentially effective compound against bacterial infection, antibiotic resistance, and biofilm formation.