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The AHR: from a xenobiotic sensor to a Pattern Recognition Receptor, playing a role in immunity to infection and drug-therapy

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Abstract

Background: The interaction between a bacterial pathogen and its host can be viewed as an "*arms race*" in which each participant continuously responds to the evolving strategies of the other partner. A mechanism allowing bacteria to rapidly adapt to such changing circumstances is provided by density-dependent cell-to-cell communication known as *Quorum Sensing* (QS). QS involves a hierarchy of signalling molecules, which in pathogenic bacteria is associated with biofilm formation and virulence regulation. **Objective:** We hypothesized that if a host sensor can detect and differentiate between bacterial QS molecules and their expression patterns, it will allow hosts to customize their immune responses according to the stage and state of infection. **Methods:** We have implied *in vitro* and *in vivo* assays (e.g., mouse, zebrafish) to evaluate how the host senses and responds to bacterial QS. **Results:** We found that the Aryl Hydrocarbon Receptor (AHR), a well-recognized receptor in the field of Toxicology, plays a role as an Innate Immune sensor. The AHR is able to sense diverse microbial-derived ligands and regulate different host defence mechanisms, according to the status and type of infection [1]. AHR modulation depends on the relative abundances of different QS molecules, whereby their quantitative assessment enables the host to sense bacterial community densities that may have distinct gene expression programs and infection dynamics. **Conclusions:** This study brought together concepts of immunology, which focused on the mobilization of defence mechanisms that combat invading pathogens, and concepts of toxicology focused on detoxification responses to inactivate toxins. We propose that by spying on bacterial *quorum*, the AHR acts as a major sensor of infection dynamics, capable of orchestrating host defence according to the *status quo* of the infection [1, 2]. Furthermore, our studies implicate the AHR in antibiotic resistance, whereby AHR activation by both drugs and infection impacts therapeutic efficacy [3].

Keywords: AHR; PRR; host-microbe interactions; quorum-sensing; antibiotic resistance

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