Genetics Day Poster Submission

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Title: ARYL HYDROCARBON RECEPTOR ACTIVATION ALTERS MONOCYTIC CELL RESPONSES DURING CORONAVIRUS AND INFLUENZA A VIRUS INFECTION

Abstract: Respiratory viruses pose a significant threat to global health, causing morbidity, mortality, and socioeconomic loss. One mystery associated with respiratory viral infections, such as with influenza A viruses (IAV) and coronaviruses (CoV), is the broad variability in disease severity that is observed, even during outbreaks of the same strain. Environmental exposures are a likely contributing factor; however, the cellular mechanisms that explain connections between exposures and variable outcomes are poorly defined. One way through which environmental factors modify the immune response is via the aryl hydrocarbon receptor (AHR). The AHR is activated by a broad range of small molecules from the environment, including both synthetic and naturally derived substances. Ligands include certain pollutants, such as dioxins and dioxin-like chemicals, which have long been associated with altered adaptive immune responses in human population studies and animal models. However, less is known about the impact of AHR ligands on monocytic cell responses. This is important because dysregulation of monocytic lineage cells contributes to poorer clinical outcomes in IAV and CoV infections. To test the hypothesis that AHR activation influences monocytic cell responses during respiratory viral infection, mice were infected with either a human IAV or a mouse CoV, and AHR was activated using the prototype agonist, 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). Monocytic cells were examined at multiple points in time relative to infection using flow cytometry. In the absence of infection, AHR activation had no discernible impact on the percent or number of monocytes in the lung. In contrast, during IAV and CoV infection, AHR activation significantly reduced monocytes in the lung. Further, AHR activation shifted the ratio of inflammatory to patrolling monocytes, such that there were significantly more inflammatory monocytes. Upon recruitment to the lung, monocytes regulate inflammation and aid in tissue repair, however, they can also differentiate into interstitial macrophages and dendritic cells (moDCs). AHR activation significantly reduced lung moDCs and interstitial macrophages during infection. Moreover, AHR activation diminished the frequency of circulating monocytes in infected, but not naïve, mice. These findings indicate that AHR activation disrupts multiple aspects of monocytic cell responses during infection, offering new perspectives on the role of AHR-binding chemicals in seasonal and pandemic viral outbreaks. Monocyte dysregulation has been

implicated in the pathogenesis of many diseases, including arthritis, diabetes, multiple sclerosis, and chronic lung diseases. Thus, AHR modulation of monocytes has the potential to affect the course of many diseases. on the bioplastic gives users control over when and how quickly the biopolymer degrades. In the near future, we will integrate marine biodegradable polymers into the blue economy.