Fall 2024

Biochemistry and Molecular Biology Brown Bag Series

Mili Bhakta

"AhR expression negatively regulates the IgH gene expression in a human B-cell line"

Tuesday, September 24, 2024

11:00 AM

Location 105 Biological Sciences Building

Lab: Courtney Sulentic, Ph.D.

Boonshoft School of Medicine
WRIGHT STATE UNIVERSITY

WRIGHT STATE UNIVERSITY

https://science-math.wright.edu/biochemistry-and-molecular-biology

Abstract

Aryl hydrocarbon receptor (AhR) mediates the immunosuppressive effects of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) in murine B cells. Our previous studies utilizing a human Burkitt lymphoma cell line (CL-01) demonstrated an inhibitory effect of AhR activation on γ and ε expression (i.e. coding for IgG and IgE, respectively) but no effect on μ and α (i.e. coding for IgM and IgA, respectively). Notably, AhR knock-down by siRNA or CRISPR/Cas9 gene editing resulted in a marked loss of IgG secretion, but IgM secretion remained unaffected. To determine if AhR regulates transcription of IgG, we utilized another human B-cell line (SKW 6.4) originating from a different, non-related Burkitt's lymphoma that lacks endogenous expression of AhR. SKW WT cells, like CL-01 AhR-KD cells secrete significantly lower levels of IgG compared to CL-01 WT cells suggesting that AhR plays a critical role in IgG production. We hypothesized that expression of the AhR in the SKW 6.4 cells would result in expression of IgG. Therefore, we created a SKW AhR+ clone that stably expresses AhR via lentiviral transduction. Contrary to CL-01 cells, induction of AhR expression in SKW AhR+ cells did not induce IgG production. However, IgM secretion was significantly inhibited in SKW AhR+ cells as compared to SKW WT cells. At the transcript level, we observed that the expression of all isotypes (μ, γ, α, and ε) was inhibited in SKW AhR+ cells compared to SKW WT cells. These observations suggest that expression of AhR (in absence of a ligand) negatively impacts the transcription of the *IgH* gene in SKW cells. Overall, our study suggest that AhR has a ligand-independent effect on human *IgH* gene expression and antibody production.