**IDENTIFICATION OF POTENTIAL ENDOGENOUS LIGANDS FOR CD14.**

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**BACKGROUND:** CD14, a myeloid cell differentiation antigen expressed predominantly on the surface of monocytes and macrophages, plays a prominent role in innate immunity, particularly as a receptor for LPS and a component of the TLR4-MD2 receptor complex. Interestingly, mice lacking CD14 are highly resistant to the lethal effects of LPS as well as to infection with Gram-negative bacteria. We hypothesize that CD14 may have additional functions and thus we screened a human brain cDNA library to identify potential endogenous ligands using the yeast-two hybrid (Y2H) system.

**METHODS:** The bait vector was constructed by cloning the human CD14 gene into the yeast bait vector pGBKT7 (Clontech), This “bait” vector was used to screen the human brain cDNA library (Clontech). The clones that contained interacting proteins grew on media that had antibiotic aureobasidin and interaction was defined by a blue color due to the presence of X-alpha-gal substrate.

**RESULTS:** This screen resulted in the identification of 55 different potential endogenous ligands for CD14, several of which are known to be involved in different aspects of inflammation. One of these ligands, PON2, has antioxidant properties and has connections to Alzheimer’s Disease and atherosclerosis. An S311C polymorphism in the 3’ fragment of PON2 seems to be related to a weaker interaction with CD14.

**CONCLUSIONS:** Y2H screening has allowed us to identify 55 new potential ligands for CD14. We are now using different techniques to test the strength of the interactions of several of these ligands and to verify the interactions biochemically by Western blot. In the long term we will test the importance of these interactions in functional assays.

**CONTENT CATEGORY:** Basic and translational science.

**KEYWORDS:** *Y2H, inflammation, atherosclerosis, brain, CD14*