Specific Aims

Prader-Willi Syndrome (PWS) is a complex, multisystem genetic disorder resulting from a deletion on the paternal chromosome 15 that occurs between the 15q11-q13 region in which there are 5 imprinted genes expressed only from the paternal chromosome (1). One of these genes, necdin (NDN) has been found to play a primary role in neural tissue differentiation having many effects in the organism, many of which have been well studied (2). Because NDN has multiple roles in the system, its deletion in PWS may contribute to many of the different symptoms of the disorder. NDN is found only in mammals and thus, Mus musculus has been the primary model organism used in studies. Mus musculus NDN has shown to have expression solely in the brain in comparison to the ubiquitious expression found in Homo sapiens NDN (3). Our **knowledge gap** is then if the knockout of the ubiquitous expression of Homo sapiens NDN leads to loss of different functions within the organism with PWS than in Mus musculus.

Our **primary goal** is to discern the differences and similarities between the Homo sapiens, Mus musculus, and Macaca mulatta NDN homologues with hopes of Macaca mulatta being a more informative study organism for PWS.
Indeed, our **hypothesis** is that Macaca mulatta NDN will show more similar expression patterns and phenotypes to Homo sapiens than Mus musculus does because of its closer evolutionary split and similarity between sequences.
In studying this, our **long term goal** is to determine how Homo sapiens NDN mutation creates specific symptoms of PWS in humans in order to create better drugs and/or treatment options.

Aim 1: Determine basic similarities and differences of Homo sapiens, Mus musculus, and Macaca mulatta NDN
Approach: Use BLAST, SMART, and UniProt to determine gene and protein sequences and compare across species.

Aim 2: Determine locations of expression of NDN protein in Macaca mulatta
Approach: Use Immunohistochemistry biomarkers to determine presence of NDN throughout Macaca mulatta tissue in comparison to Mus musculus and Homo sapiens from past studies

Aim 3: Create NDN-null mutant Macaca mulatta in order to determine basic mutant phenotypes
Approach: Use CRISPR technology to knockout NDN in Macaca mulatta

Studies on Macaca mulatta have been increasing in terms of genetic imprinting. We hope that by using Macaca mulatta, a more similar organism to Homo sapiens, to study the effects of the loss of NDN, we may be able to determine further areas of study for PWS defects.

References
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2) Macdonald, H., & Wevrick, R. (1997). The Necdin Gene is Deleted in Prader-Willi Syndrome and is Imprinted in Human and Mouse. *Human Molecular Genetics,6*(11), 1873-1878.
3) NDN - Necdin - Homo sapiens (Human). (n.d.). Retrieved February 26, 2015, from http://www.uniprot.org/uniprot/Q99608