Milestone	Task	Year 1		Year 2		Year 3		Year 4		Year 5	
		Jan-Jun	Jul-Dec	Jan-Jun	Jul-Dec	Jan-Jun	Jul-Dec	Jan-Jun	Jul-Dec	Jan-Jun	Jul-Dec
Aim 1 - Hypothesis-based candidate gene approach											
Aim 1.1 Study signal transduction pathways in tissue samples	Collection of specimens from affected subjects	███	███	███							
	Test production of candidate genes under various assay conditions		███	███	███	███					
(Plan for non-responders/negative samples)	Confirm or exclude candidate gene defect in negative samples using other assays		███	███	███	███					
	Define the candidate genes in these specimens by investigating other signaling pathways		███	███	███						
(Plan for samples with positive response)	Additional testing for other signal transduction pathway production in assays			███	███	███	███				
	Further analysis of signal transduction pathway under variety of assay conditions				███	███	███				
Aim 1.2 Identify and characterize predisposing mutations involved in signaling pathways	Define candidate genes in patient samples with impaired function				███	███	███	███			
	Sequence genomic exons and coding regions of correponding cDNAs				███	███	███	███			
	Determine corresponding levels of gene expression and protein production with real-time PCR and Western Blotting					███	███	███	███		
	Validate mutations by assessing the intrafamilial segregation of the allele and its frequency in the general population					███	███	███	███		
Aim 2 - Hypothesis generating genome-wide strategy of homozygosity mapping											
Aim 2.1 Map linked chromosomal regions by genotyping genome of consanguineous families & analyzing data by homozygosity mapping	Recruit consanguineous kindreds/receive blood and skin samples					███	███	███	███	███	███
	Conduct positional cloning					███	███	███	███	███	███
	Identify homozygous regions linked with candidate gene					███	███	███	███	███	███
Aim 2.2 Identify and characterize mutations in genes located in chromosomal regions linked with candidate gene	Select candidate genes					███	███	███	███	███	███
	Investigate role of candidate genes in the regions of interest					███	███	███	███	███	███
	Sequence coding regions					███	███	███	███	███	███
	Assess protein expression by Western Blotting & mRNA expression by qRT-PCR in cell samples					███	███	███	███	███	███