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Fusarium head blight (FHB) or scab, is a disease of economic importance affecting small grain crops every year causing billion dollars of loss in grain quality as well as quantity. Although many Fusarium species can cause FHB, *Fusarium graminearum* Schwabe [teleomorph = *Gibberella zeae* (Schwein) Petch] is the primary pathogen responsible for recent epidemics in the United States. FHB affects the developing heads of wheat directly and has been regarded as a severe threat to U.S. and global food security. A strong need has always been felt for long term commitment of combining wheat scab resistance with desired agronomic traits in commercial wheat cultivars. It is not completely possible without a clear and fundamental understanding of wheat's defense response to scab infections at molecular levels. In a plant cell, the genes are translated into proteins to perform a function; or in other words proteins are the actual (functional) players inside the plant's cell for a particular phenotype (e.g. scab resistance or susceptibility). Given the complexity of breeding for FHB resistance, identification of molecular functional markers and the discovery of FHB responsive genes associated with FHB resistance will be a valuable knowledge in accelerating efforts to breed FHB resistant wheat cultivars. These "omics" kind of experiments in wheat were limited so far because of non-availability of its genome sequence. A recent announcement of availability of wheat genome sequence, availability of recombinant inbred lines (RILs) and availability of cutting edge proteomic technology is that combination which persuades us to mine the wheat proteome to get the molecular insights of wheat defense mechanism against FHB. The newly discovered genes will have a potential of utilization to increase resistance to FHB in wheat as well as other small grain crops through either conventional plant breeding or through transgenic strategies. Thus the central theme of this project is to seek a comprehensive and fundamental knowledge with the discovery of FHB responsive genes in wheat upon Fusarium infections. The young heads of resistant and susceptible recombinant inbred lines will be challenged with Fusarium and the infected heads will be subjected to cutting-edge iTRAQ technology for the discovery of *Fusarium* responsive wheat proteins. The key proteins will be identified through LC-MS/MS technology. For this purpose, a large wheat EST database and recent availability of wheat genome sequence is especially helpful. On a short term objective we look for the discovery of *Fusarium*-responsive wheat genes and characterization of at least 10 most differentially regulated proteins/genes associated with FHB resistance mechanism. On a medium and long term goal – the identified genes will be expressed and accumulated in *Fusarium*-sensitive lines to study function of newly discovered functional genes. We plan to validate the newly discovered genes and test them in wheat background in the subsequent years.