Our body equips a cytoprotective system that senses environmental insults and activates cellular defense enzyme genes. Transcription factor Nrf2 is essential for the coordinated induction of cellular defense enzymes through antioxidant/electrophile responsive element (ARE/EpRE). This notion has been best demonstrated in animal models, showing that Nrf2-null mice are sensitive to a wide variety of electrophiles and ROS. Keap1 is a component of ubiquitin-E3 ligase that degrades Nrf2 constitutively. Keap1 possesses reactive cysteine residues that act as sensors for electrophilic and oxidative stresses. We refer to this system as the Cysteine Code. The two-site recognition/hinge and latch model proposed for the Keap1-Nrf2 system describes the mechanism of nuclear accumulation of Nrf2 in a Cul3-Keap1 E3 ubiquitin ligase-dependent manner. We have verified this model through structure biology, mouse/zebrafish genetics, and human cancer analyses. In human cancers missense mutations have been identified in KEAP1 and NRF2 genes. These mutations disrupt the KEAP1-NRF2 complex and result in constitutive activation of NRF2. Elevated expression of NRF2 target genes confers advantages on the growth of cancer cells through the Metabolic Reprogramming. Transgenic mouse models provide evidence that mutated form of Keap1 analogous to cancer genotypes lose the ability to repress Nrf2 \textit{in vivo}. Thus, the Keap1-Nrf2 system opens a new avenue to the understanding of the signal transduction and regulatory processes underlying the stress response and cancer progression.