Between the 50s and 80s, protein degradation was a neglected area. While it was recognized that proteins turn over, the high specificity of the process - where distinct proteins are degraded when they are damaged or completed their function, was not appreciated. The discovery of the lysosome that degrades proteins in bulk did not solve the enigma that was solved only with the discovery of the ubiquitin system. Degradation of cellular proteins via this system is highly regulated and plays major roles in all cellular processes. With multitude of substrates targeted, aberrations in the pathway have been implicated in the pathogenesis of many diseases, malignancies and neurodegenerative disorders among them, and the system has become a major platform for drug development.