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Over the past decade, a group of researchers from 4 institutions, Institute of Fundamental Technological Research of the Polish Academy of Sciences, Silesian University of Technology, University of Texas Medical Branch, and Rice University, have developed multidisciplinary research in experimentation, computational modeling and bioinformatic analysis of the NF-kB signaling module and its neighbors, the p53 and interferon b pathways. The techniques employed range from cell and molecular biology experiments, high-content microscopy and DNA microarrays, through stochastic simulation, bioinformatics and paper-and-pencil mathematics. Collaboration involves exchanges with researchers from Stanford University, Los Alamos Laboratory, and the Universities of Warwick, Manchester and Heidelberg. It has been funded by grants from Polish and US funding agencies. In the talk, I will present basic information about the NF-kB, its role in innate immunity and connections with other pathways. This will be followed by a brief discussion of novel stochastic, deterministic and spatial models of response to pathogens that were developed based, among other, on single-cell experiments. Evolutionary studies helped in understanding the promoter structure of the NF-kB-dependent genes and the temporal patterns of their response. In particular, I will discuss the model of the NF-kB and RIG-I-MAVS cross-talk, which is currently under development.