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Noisy information processing in the innate immune response

The cellular recognition of viruses evokes the secretion of type-I interferons. in turn, interferons trigger an antiviral response that limits viral replication and spread. Combining the imaging of interferon induction and response in single cells with mathematical modeling, we uncovered strong cell-to-cell heterogeneity at multiple levels of regulation. The initiation of antiviral signaling, the induction of IFN genes and the expression of viral restriction factors all display large variability across a clonal, homogeneously infected cell population. We show that much of this variability is due to cell-intrinsic noise. We predict theoretically, and verify experimentally, that a small fraction of IFN-producing is sufficient to induce IFN target genes in the other, non-producing cells of the population. The coupling of the stochastic sensing of viral infections by the innate immune system with the paracrine amplification of protective responses has implications for our understanding of the biology of viral diseases.