All forms of life have established sophisticated mechanisms to detect and eliminate foreign genetic material. Research on the molecular pathways that keep foreign pathogen-derived nucleic acids in check has followed three principle directions: pattern recognition, nucleic acid restriction factors, and nucleic acid metabolism. However, current advances have led us to understand that they are all integral parts of a larger nucleic acid defense system, which now is referred as Nucleic Acid Immunity. Nucleic acid metabolism relies on nucleases and other components of nucleic acid metabolism pathways that regulate the abundance or composition of nucleic acids. Important examples include nucleases such as TREX1, DNase II, components of the RNA exosome complex or proteins of the nucleotide metabolism such as SAMHD1. This talk will provide an overview of nucleic acid immunity and our recent insight in the role of endolysosomal DNases and RNases in the regulation of nucleic acid immune sensing.