Is it Time for Computation-driven Drug Design? The Discovery of a Small Molecule STING Agonist using the QUAISAR Computational Platform

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The STING protein induces type I interferon (IFN) production upon activation by abhorrent DNA from pathogens or tumors. Here, we describe the rational design of a novel small molecule STING agonist with favorable drug-like properties that shows a robust in vivo anti-tumor response. To account for the unique dimerization binding mechanism of action, bespoke computational methods were developed (QM, MD, and AI/ML). The clinical compound (SNX281) was engineered by computationally exploring millions of virtual molecules but synthesizing only 200 small molecules in the lab. We will also highlight how this approach is being applied more broadly across a variety of inflammation and oncology targets.