

Discovery of Dual-Acting Compounds as NAMPT Inhibitors and SIRT1 Activators through Sequential Virtual Screening

Fikriye Ozgencil¹, Selen Ozge Almamis², Huseyin Cimen², Alberto Massarotti³, Gokcen Eren¹

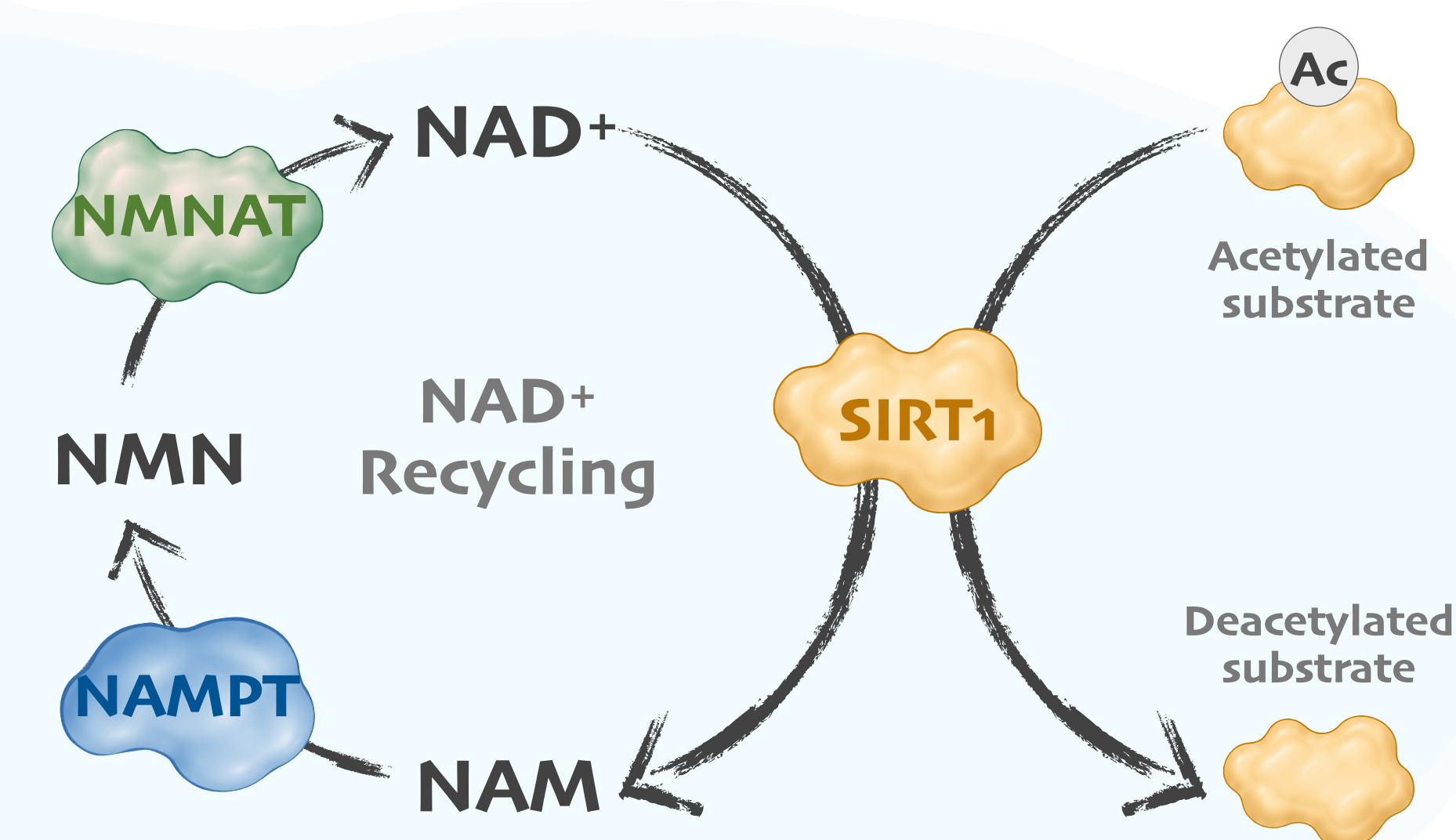
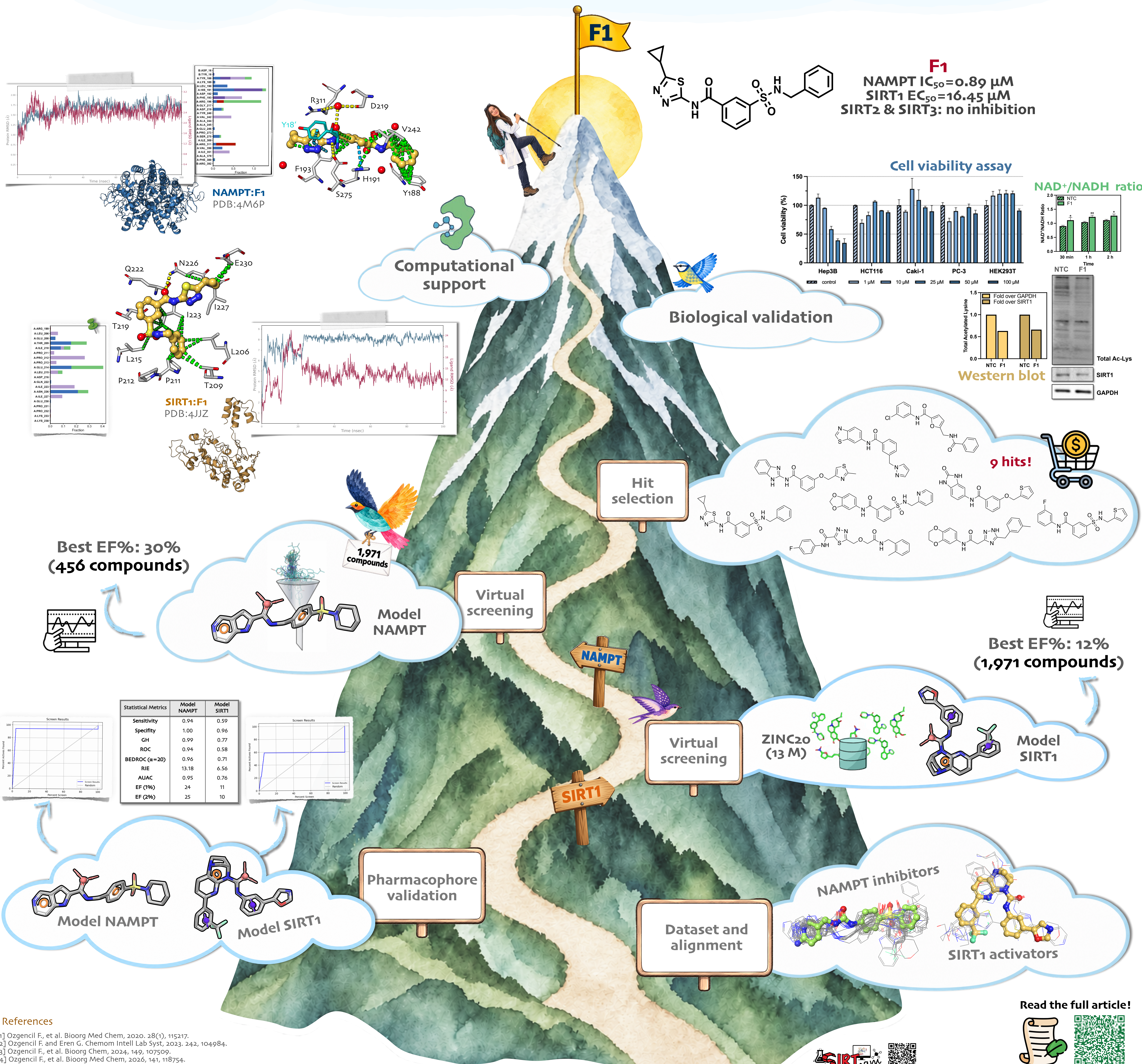
¹Gazi University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, SIRTeam Group, Ankara, Türkiye 🇹🇷

²Gebze Technical University, The Institute of Biotechnology, Kocaeli, Türkiye 🇹🇷

³Università degli Studi del Piemonte Orientale "A. Avogadro", Dipartimento di Scienze del Farmaco, Novara, Italy 🇮🇹

Cancer cells exhibit increased metabolism, growth, and activity of **NAD⁺**-consuming enzymes, resulting in rapid **NAD⁺** depletion and greater sensitivity to **NAD⁺** deficiency than normal cells. Therefore, **NAMPT**, the rate-limiting enzyme in the major **NAD⁺** biosynthesis pathway, has emerged as a promising anticancer target. However, the dose-dependent toxicity and adverse effects of NAMPT inhibitors have increased interest in **multi-target strategies**. **SIRT1** is an **NAD⁺**-dependent deacetylase involved in DNA repair, gene expression, and cell death. The functional relationship between NAMPT and SIRT1 through the **NAMPT-NAD⁺-SIRT1 axis** provides a rationale for their simultaneous modulation [1-4].

Therefore, we aimed to identify bifunctional compounds capable of simultaneously **inhibiting NAMPT** and **activating SIRT1** as a dual-targeting strategy [4].



References

- [1] Ozgencil F, et al. Bioorg Med Chem, 2020, 28(1), 115217.
- [2] Ozgencil F and Eren G. Chemom Intell Lab Syst, 2023, 242, 104984.
- [3] Ozgencil F, et al. Bioorg Chem, 2024, 149, 107509.
- [4] Ozgencil F, et al. Bioorg Med Chem, 2026, 141, 118754.

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