**SYNTHESIS OF POTENTIAL IRE1α INHIBITORS**

**POTENCIĀLU IRE1α INHIBITORU SINTĒZE**

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Cancer has a major impact on society around the world and it is one of the leading causes of death. IRE1α is an enzyme that plays a part in the development of certain cancers, such as breast cancer, colon cancer, and prostate cancer. IRE1α inhibitors might be used to treat these types of cancer. [1]

The aim of this study was to find IRE1α inhibitors that would have a greater selectivity and bioavailability than the previously discovered ones. Based on computational data about the activity of compound 4f, it was chosen as the model compound for further synthesis.



**Fig. 1.**  Synthesis of target compounds **4a-f**.

The reaction used for the synthesis of compound 4f and its analogues was found to yield endocyclically acylated 1,2,4-triazol-5-amines instead of the anticipated exocyclically acylated compounds, but isomerization of endocyclically acylated 1,2,4-triazol-5-amines yielded exocyclically acylated compounds. However, limited hydrolytic stability of compounds 3a-f suggested that the inhibitory activity of these compounds could be mainly due to the presence of compounds 2a-f in solution. Indeed, compound 2f had the greatest ability to inhibit IRE1α out of all the synthesized compounds.

***References:***

[1] Madden, E.; Logue, S. E.; Healy, S. J.; Manie, S.; Samali, A. The Role of the Unfolded Protein Response in Cancer Progression: From Oncogenesis to Chemoresistance. Biol. Cell 2019, 111 (1),
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