CHRONIC AUTOIMMUNE AND INFLAMMATORY DISEASES – THE PROBLEM

Chronic autoimmune and inflammatory diseases such as **rheumatoid arthritis, other autoimmune diseases** and **chronic inflammatory lung** diseases affect a large number of people worldwide.

The prevalence of rheumatoid arthritis alone is estimated to reach approximately 1% of the human population and is characterized by joint inflammation leading to cartilage damage and bone resorption, and subsequent bone deformation and loss of joint function. Similarly, other inflammatory diseases such as **other autoimmune diseases** or **chronic inflammatory lung diseases** are also devastating **chronic diseases.** Due to their chronic course, those diseases lead to permanent and severe reduction in the quality of life.

Despite the high prevalence and public burden of chronic autoimmune and inflammatory diseases, current therapeutic options are still very limited and associated with major side effects and very high costs. Therefore, development of new therapeutic strategies to combat **chronic autoimmune and inflammatory diseases** are warranted and has been given high priority by the biomedical and pharmaceutical industry.

Src family kinases are non-receptor tyrosine kinases involved in diverse biological functions. Their role in cellular proliferation and invasion, the high frequency of gain-of-function mutations in **Src family kinase genes** in tumors, and the presence of their oncogenic variants in oncogenic viruses indicate a role of those kinases in malignancies. Those findings triggered significant efforts aimed at therapeutic targeting of **Src family kinases** in human cancer, resulting in the development of several small-molecule **Src family kinase inhibitors** that showed very promising effect in human oncology patients during the last several years. **Src-family kinases** are also involved in various functions of immune cells but their role in **inflammatory diseases** and the possibility of their **therapeutic targeting** in those diseases have not been widely appreciated yet.

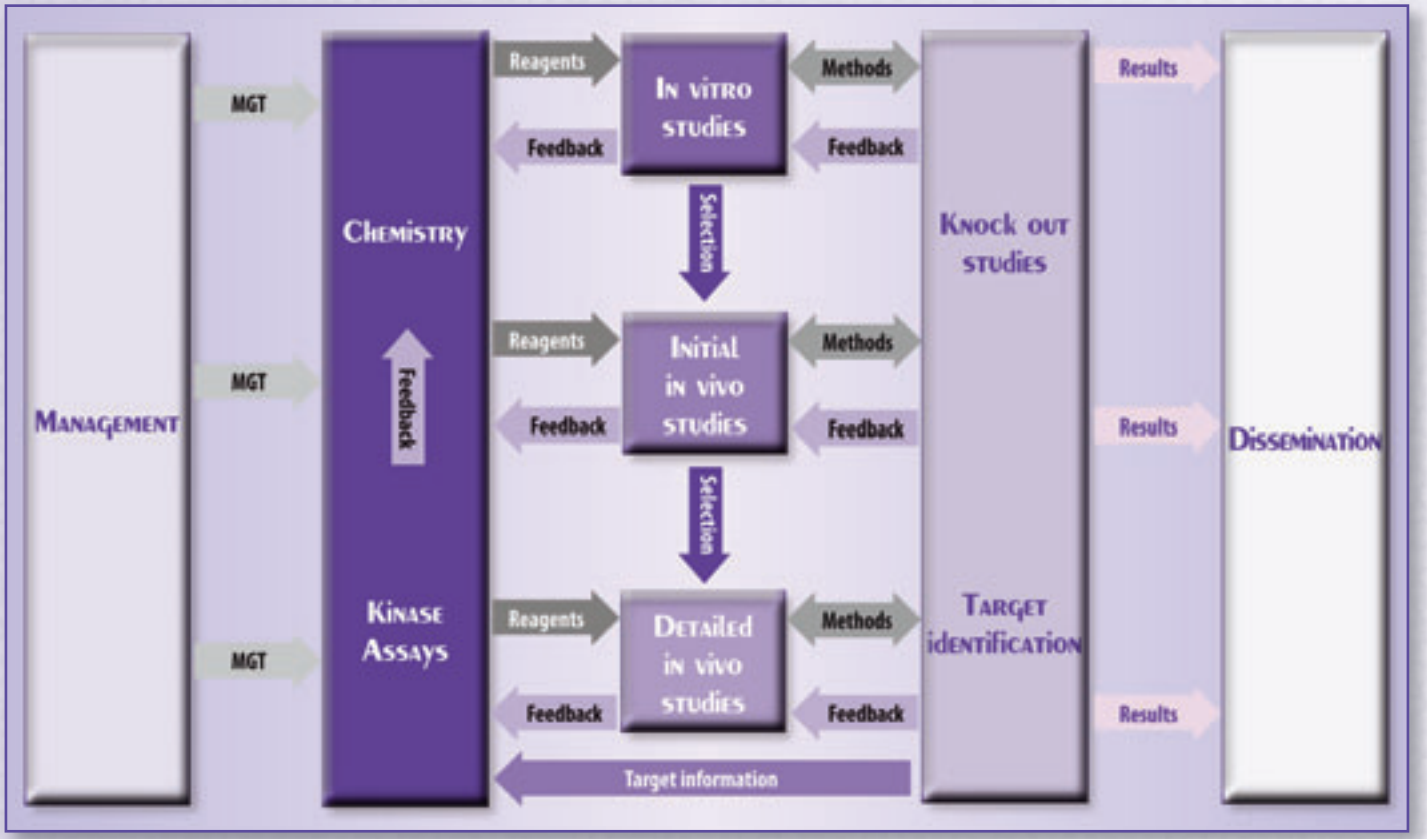
TARKINAID FOCUS AND OUTCOME

The TARKINAID project aims to develop **novel small molecule anti-inflammatory compounds** based on the inhibition of **Src family kinases** in inflammatory cells. Using genetic approaches, members of the **TARKINAID consortium** have previously shown that **Src family kinases** are indispensable for a number of inflammation-related in vitro functions of leukocytes, as well as for the development of various in vivo animal models of autoimmune inflammatory diseases. The **TARKINAID consortium** has also identified a number of novel small-molecule kinase inhibitors that inhibit members of the **Src kinase family** and block in vitro neutrophil functions. Those molecules serve as lead compounds for further drug optimization.

The core part of the **TARKINAID project** consists of the pre-clinical evaluation of novel **Src family kinase inhibitors** in various animal models of **chronic autoimmune and inflammatory diseases.** This core part will be supported and preceded by a series of in vitro and additional in vivo assays to predict and optimize the most promising inhibitors and test their safety and pharmacokinetic properties.

TARKINAID ALLIANCE

The **TARKINAID consortium** consists of eleven members (including four SMEs) from six different countries. As part of an EU-sponsored **network between European and Brazilian scientists,** two group leaders are from **Brazil.** To promote research in **Eastern-European countries,** the coordinator and one SME are from **Hungary.**



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TARKINAID

Targeting Src-family tyrosine kinases in chronic autoimmune and inflammatory diseases