Surprisingly, only 1.5% of the mammalian genome encodes proteins, the remainder being non-coding DNA. In recent years, it has been discovered that part of it is transcribed, resulting in the formation of non-coding RNA. One class of such transcripts are long non-coding RNAs (lncRNAs), which are more than 200 nucleotides in length, do not encode proteins, but undergo the RNA maturation processes characteristic of coding transcripts. They interact with DNA, RNA, and proteins, and perform important biological functions such as the regulation of transcription, protein synthesis, intron excision, cytoplasmic and nuclear transport. A change in the expression profile of long non-coding RNAs in mammalian cells has been observed in the course of various diseases, including viral diseases, including those caused by the influenza virus. Some long non-coding RNAs promote multiplication of the influenza virus by suppressing the cellular immune response, others alter cell metabolism to promote viral replication. In recent years, cellular long non-coding RNAs have been identified that are essential for influenza virus multiplication and are not involved in modulating the immune response, some of which interact directly with influenza proteins.

In this research project, we plan to take into account the fact that the structure of the long non-coding RNAs necessary for influenza virus propagation is still little understood, and the structural motifs present in the long non-coding RNAs may play an important role in viral biology. Therefore, the main goal of our project is to study the structure of selected long non-coding RNAs for the presence of functional RNA motifs and to study their potential impact on the replication cycle of the influenza virus. To this end, we plan bioinformatics studies that will identify potential functional RNA motifs present in selected long non-coding RNAs. In the next stage, we will perform structural studies of RNA mapping both in vitro and in infected cell lysates that reflect cellular conditions. In the third stage of the project, we would like to determine the role of potentially functional RNA motifs of long non-coding RNA in the replication cycle of the influenza virus and we will perform in vitro biological studies using influenza A infected cells. More specifically, we will introduce mutations that alter the structure of long non-coding RNAs in potentially functional structural motifs, and then examine how these changes affect the influenza virus replication cycle. In the last part of the project, we will use the knowledge of RNA motifs of long non-coding RNA to inhibit the replication of influenza virus in several cell lines. We will use RNA modulating and structure dependent tools such as antisense oligonucleotide (ASO), small interfering RNA (siRNA), and the CRISPR/Cas strategy. In the case of ASOs, siRNAs, and the components of the CRISPR/Cas system that best inhibit the multiplication of the influenza virus will be examined in terms of possible cytotoxic effects on cells.

The proposed research will allow increase the knowledge about the structure of long non-coding RNAs necessary for efficient the multiplication of the influenza virus. The results of our research will provide detailed information on the occurrence of functional RNA motifs of long non-coding RNAs and their structure, as well as the potential biological function that they may play in influenza virus replication. Moreover, we will develop tools that inhibit the multiplication of the influenza virus in cell lines. The results obtained may be useful in the further development of new antiviral strategies targeting the long non-coding RNAs used by the influenza virus to carry out its replication cycle.