RATIONAL APPROACH FOR SEARCHING MOLECULAR TARGETS INVOLVED IN INFLAMMATORY EVENTS AND CELL SURVIVAL

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ABOUT THE PROJECT

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Successful drug development requires a disease target that plays a vital role in the causation and/or progression of the disease phenotype and that can be modulated with a drug molecule. In other words, therapeutically relevant targets are both "disease-modifying" and "druggable". It has been estimated that around 10% of the entire human genome is involved in disease onset or progression, resulting in approximately 3000 potential targets suitable for therapeutic intervention. Thus, the rapid and reliable identification of the most promising targets for drug discovery efforts would be the major challenge for the pharmaceutical industry. Moreover, the knowledge of the mechanisms that govern the inflammatory process and cell survival, generated by basic research, is essential for the identification and validation of potential and more specific molecular target. Natural products are a rich source of biologically active compounds. Many of today's medicines are either obtained directly from a natural source or were developed from a lead compound originally obtained from a natural source. Venoms and toxins from animals, plants, snakes, spiders, scorpions, insects, slugs, and microorganisms are extremely potent because the often have very specific interactions with a macromolecular target in the body. As a result, they have proved to be important not only as lead compounds in the development of novel drugs, but also as tools in studying receptors, ion channels, and enzymes. In our research group, interesting bioactive molecules from animal venoms and secretions, such as proteins (wild or recombinant form) and derived-peptides, targeting the homeostatic system and inflammatory events, have been exploited and are in different phases of development. We have been focusing our efforts on understanding their mechanism of action through the exploitation of specific signaling pathways in order to identify and validate novel molecular targets. Among the proteins' families taken into account are lipocalins, hemolins, serine protease inhibitors, phospholipases and chaperones. In this regard, the main idea is to consider the expertise of the Butantan Institute researchers already have in computer-aided molecular design/bioinformatics/OMICS (transcriptome, proteome) field, molecular and cellular biology and immunology approaches (in vitro assays), and in vivo models and image techniques in order to create a Center of Excellence for Research in Target Discovery.