

PREFACE

I started my research work in 2009 under the supervision and expert guidance of Prof. T. K. Chaudhuri and co-supervision of Dr. Soumen Bhattacharjee, Department of Zoology, University of North Bengal, and Dr. Biswajit Halder, Department of Pathology, North Bengal Medical College and Hospital, Sushrutnagar, Dist. Darjeeling. My entire work has been documented in this dissertation entitled “STUDY OF THE GENETIC DIVERSITY OF KILLER CELL IMMUNOGLOBULIN LIKE RECEPTORS (KIRS) IN SOME HUMAN POPULATIONS OF SUB-HIMALAYAN REGION”.

Killer-cell immunoglobulin-like receptors (KIR) constitute a family of receptor molecules that are present on both natural killer (NK) cells as well as on a subset of T-lymphocytes. The nomenclature of these receptors is based on the number of extracellular immunoglobulin-like domains (2D or 3D) and the character of the cytoplasmic tail (L or S). KIRs with long cytoplasmic tails are involved in inhibitory signaling while those with short cytoplasmic tails transduce activation signals. The members of the KIR family interact with human leukocyte antigen (HLA) expressed on the surface of all nucleated cells. Normal KIR/HLA interaction protect the cell against cytotoxic effects of NK cells, failure of which may result in positive intracellular signals. These resulting signals affect NK cell activity causing the release of cytotoxic enzymes. Thus, KIR-HLA interaction plays a major role in innate immunity. The KIR genes are highly polymorphic and are located on the long arm of chromosome 19, within the Leukocyte Receptor Complex (LRC). KIR gene content and haplotypes vary between ethnic cohorts and individuals within a population. Based on all these unique features, KIR has gained importance parallel to other established markers in the fields of human genetic diversity, in tracing the routes of human migration in different parts of the world and also in disease researches.

The sub-Himalayan part of India is inhabited by many tribes and castes each having their own cultural and linguistic ethnicity. In one hand, some populations in this region arose

due to blending of gene pool of different population groups while; on the other hand, some other populations of this region are strictly endogamous with a highly conserved gene pool of their own. In other words, it can be said that the sub-Himalayan part of West Bengal, India, is a melting pot of different ethnicity and is therefore extensively rich in genetic diversity. The present study was designed with the broad objective to study the KIR gene profile in different ethnic populations inhabiting the northern part of West Bengal. In addition, we also aimed to study association of KIR genes with Rheumatoid arthritis, which is one of the most common autoimmune debilitating diseases, affecting nearly 1% of the total world population. This disease is characterized by progressive articular damage leading to joint deformities and disability. Blood samples were collected from the volunteers with their prior informed consent. Individuals with three generations of unrelatedness were selected for the study. RA was diagnosed by the physician and the subjects were recruited from the Department of Pathology, North Bengal Medical College & Hospital, Sushrutnagar, Siliguri and 3gen diagnostic Pvt. Ltd, Siliguri. Blood samples were collected from the participants under appropriate conditions and brought to the Cellular Immunology Laboratory, Department of Zoology, University of North Bengal, where the further experiments were performed. The findings of the study are published in various research journals and are presented and discussed in details in the Results and Discussion part of this dissertation.