CHAPTER I
INTRODUCTION

Background and Rationale

Nasopharyngeal carcinoma (NPC) is a subgroup of head and neck squamous cell carcinoma. It is a rare neoplasm in Western world (less than 1 per 100,000). However, high frequencies occurs in Southern China (30-50 per 100,000), Southeast Asia (5-10 per 100,000) and Greenland Inuit (8.5-12.3 per 100,000). The incidence rate for Thais in Thailand was 3 per 100,000 case whereas Chinese in Thailand was 10 per 100,000 case.[1] The cancer was 2.5 time more frequent in male.[2]

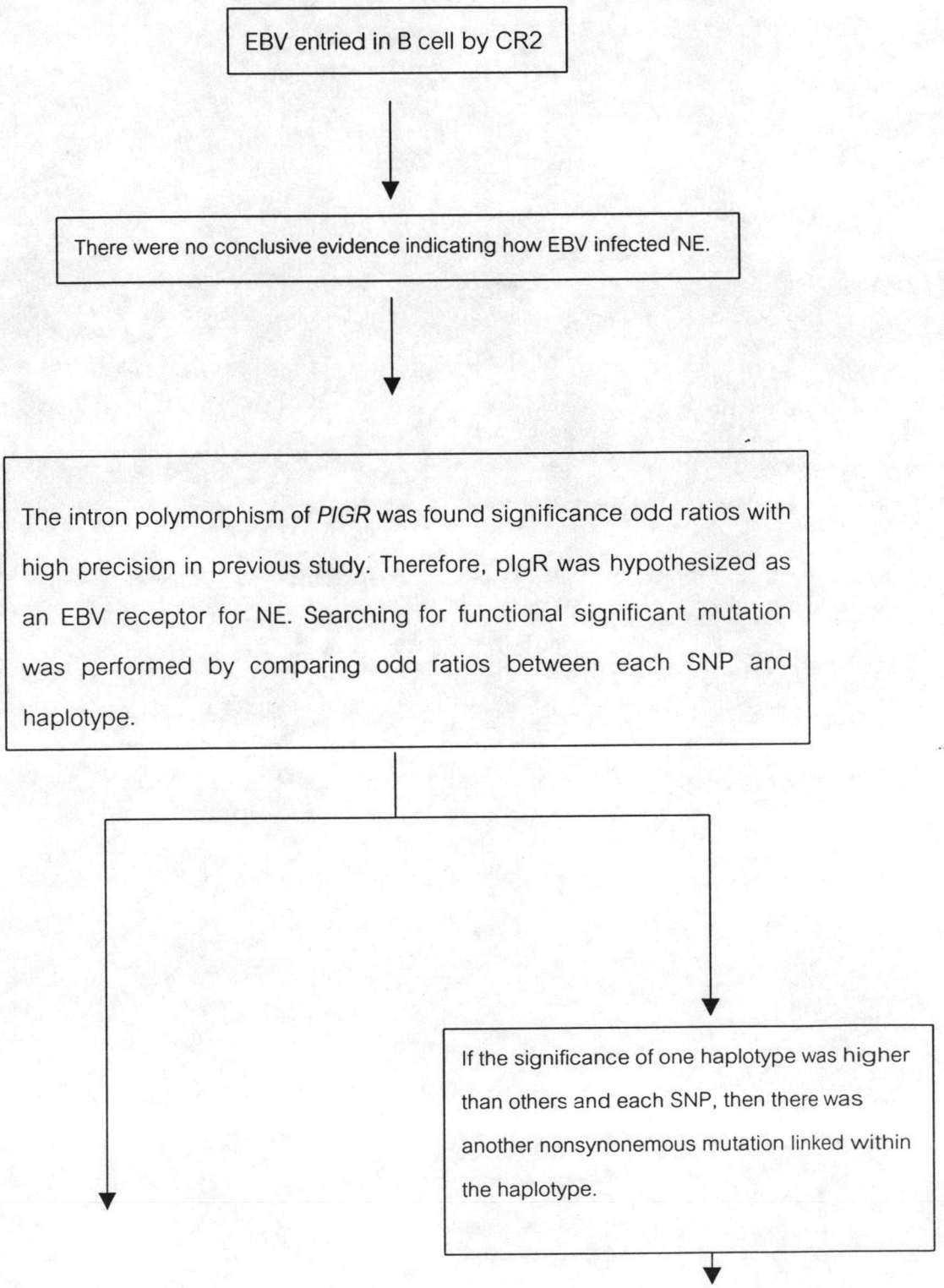
Genetic susceptibility was one of the reasons to explain the interesting endemic question why NPC was found most frequently in Chinese. Currently three genetic susceptibility loci have been reported. First, an association observed between NPC and several types of human leukocyte antigen (HLA). Southern Chinese is associated with HLA A2 and B46 [3] whereas HLA A29 in Kenyas and Tanzanians, B18 in Malays, and A3 in Australian Whites.[4,5] Secondly, polymorphisms of cytochrome P450 2E1 (*CYP2E1*), activating enzyme, which catalysed procarcinogen eliminating process, was associated with increased risk of NPC in Taiwan[6,7] and Thailand.[8] Finally, recently our research group has demonstrated that Chinese patients living in Thailand showed strongly relationship between *PIGR* intron polymorphism and the likelihood to develop NPC.[9] The ultimate goal of this thesis was to identify specific *PIGR* mutation functionally associated with the carcinogenesis by assessing the relative risks between *PIGR* single nucleotide polymorphisms (SNPs) or haplotypes in Thais, Chinese, and Thai-Chinese.

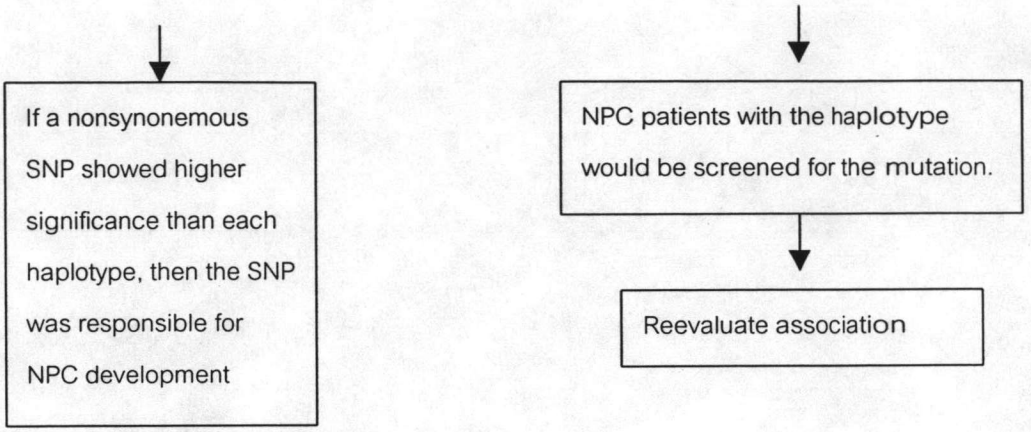
PIgR was a receptor forming secretory immune complexes with IgA or IgM and hypothesized to mediated the Epstein-Barr viral (EBV) infection of nasopharyngeal epithelium (NE). When the epithelium lost polarity or *PIGR* mutated, the viral translocation process was failed and consequently caused EBV infection.[10,11] In addition, *in vitro* study of LinCT and colleagues indicated possibility of EBV infection into NPC via pIgR-IgA complex[12] consistenly with serological studies showing high titer of EBV-IgA detection in NPC patients.[13]

Objective

Comparison SNP and haplotype of *PIGR* between NPC patients and normal control of the same ethnic in origin, Thai, Chinese and all cases including Thai-Chinese.

Conceptual Framework





Assumption

All patients and control were separated into three groups Thai, Chinese, and Thai-Chinese respectively based on their grandparent' s ethnic origin. If their ancestors, including their great grandparents, originated from China, they were considered Chinese. On the other hand, if their ancestors originated from Thailand, they were defined as Thai. If their ancestors originated from Thailand and China, they were defined as Thai-Chinese.

Limitation

Some group of patients was excluded because of the lacking of grandparents' information.

Operational Definition

-Haplotype is a genotype of a group of alleles from two or more closely linked loci on one chromosome, usually inherited as a unit.

-SNP is DNA polymorphic variation of single nucleotide.

Expected Benefit

Gather, genetic evidence if and how *PIGR* involved in NPC development. Consequently, this would be used as a guide for future NPC prevention study.

Research Methodology

1.Sample population

Sample population was categorized into two groups;

-Cases was NPC patients from Cancer Institute and King Chulalongkorn Memorial Hospital.

-Controls were blood-donating volunteers from Thai Red Cross Association

2.Blood collection and DNA extraction

3.Mutation finding by DNA sequencing

4.SNP finding

5.Primer design for ARMS and RFLP

6.PCR and gel electrophoresis

7.Polymorphism of 3' UTR analysis by polyacrylamide gel electrophoresis

8.Data collection and analysis