ABSTRACT

The neglected tropical diseases (NTD) are considered as the most disabling among the most common chronic infections of the world’s poorest population. It represents a group of chronic parasitic and bacterial infections such as hookworm infection, ascariasis, schistosomiasis, lymphatic filariosis, onchocerciasis, Chaga’s disease, leishmaniasis, and trachoma. Parasitic species of phylum nematoda are the causative agents of 6 of the 13 NTDs, which afflict around 2.7 billion people (Hotez et al 2006). Human evolution and parasitic infections have run hand in hand and had acquired an amazing number of parasites, about 300 species of helminth worms and over 70 species of protozoa. Parasitic nematodes infect nearly half the world's human population, resulting in significant morbidity and mortality. Lymphatic filariosis (LF) is a disease caused by a group of lymphatic-dwelling filarial nematodes transmitted by mosquito vectors. They are caused by three species of tissue-dwelling filaroid nematodes, such as *Brugia malayi*, *Brugia timori* and *Wuchereria bancrofti*. Approximately 120 million people (Schwab et al 2006), 2% of the world’s population in over 90 countries are infected. *W. bancrofti* is the most common causative agent and accounts for about 90% of cases while *B. malayi* accounts for 10% of cases and is confined to East and Southeast Asia. *B. timori* is found only in Timor and nearby islands. LF has been identified by the World Health Organisation (WHO) as the second leading cause of permanent and long-term disability worldwide. LF is a major
cause of morbidity, with the loss of 4.6 million DALYs (disability-adjusted life years) (Remme et al 2002), severely affecting socio-economic development in endemic areas (Ramaiah et al 2000; Zagaria and Savioli, 2002). In India, an estimated ~40 million people live in areas endemic for filariasis, with ~45 million infected individuals having both bancroftian and brugian infections. There are approximately 21 million people with symptomatic filariasis and 27 million with asymptomatic microfilaraemia, while a total of 553 million people are at risk of infection (Ramaiah et al 2000). *W. bancrofti* is the predominant species accounting for about 98% of the national burden, widely distributed in 17 states and union territories of the country (Sabesan et al 2000), with brugian infections localized to Kerala and scattered pockets of Orissa and Assam.

WHO initiated the ‘Global Program to Eliminate Lymphatic Filariasis’ (GPELF) by the year 2020, and it has been successfully implemented in China, Malaysia, Korea and certain islands of the Pacific (Ottesen 2000; Burkot et al 2002; Molyneux and Zagaria 2002). GPELF mainly focuses on mass drug administration (MDA) using either diethylcarbamazine (DEC) (Gelbrand 1994) or ivermectin (Eberhard et al 1997; Molyneux et al 2003) in single- or two-dose regime combined with albendazole once a year to interrupt transmission of LF (Molyneux and Taylor 2001; Gyapong et al 2005). However, these are micro-filaricidal drugs which cannot clear the adult worms and there is a more need for macro-filaricidal drugs. Long-lived helminth parasites have evolved highly effective
strategies to evade host immunity, which require both adaptation of existing genes and evolution of new gene families (Maizels et al 2004).

Genetic information of the parasite is essential to understand the evolution of parasite and to know the minimal set of genes and their evolution required for its survival. *B. malayi* genome is complicated by two factors: an unusually large number of singleton reads (reads that are not incorporated into the assembly); and a wide variation in the depth of coverage by reads at different regions of the genome. There is non-uniform distribution of sequence reads and the number of repeats in the tandem arrays differs, suggesting that assembly is prevented by allelic variation (Ghedin et al 2007). Large number of singleton reads of about 1,76,099 reads suggested a high A+T-rich regions (69.5%), which prevent their inclusion as a unique region of the genome (Ghedin et al 2007). The functional genes in helminths are also polymorphic and have shown a spectrum of variability, from total conservation to surprising levels of allelism even among the laboratory strains (Maizels and Atmadja 2002). Molecular polymorphisms among *B. malayi* strains have been demonstrated using microsatellite markers (Underwood et al 2000). *B. malayi* surface antigens SHP-1 and SHP-5 showed variations both at the nucleotide and amino acid levels (Maizels and Atmadja 2002). There is little evidence about the variations observed in the functional genes of *W. bancrofti*.

Genetic heterogeneity of the parasite may contribute to the observed phenotypic variation in the host–parasite interactions. There are many functional genes that play important role in the host–parasite
interaction, which help the parasites in immune evasion. The allelic variations in some of the functional genes may modify biological activity or provide diversity in the face of specific host immune response. Since such analyses are noticeably rare for any helminthic parasite, extensive study of polymorphism within protein-coding genes of potential relevance is imperative. This will be important for the proper understanding of host-parasite relationship and development of suitable diagnostic candidates and vaccines. In this study, the functional genes WbSXP-1, WbTPx-1 and WbCol-4 were selected and analyzed for polymorphism. They code for potent diagnostic antigen (WbSXP-1) and vaccine antigens (WbTPx-1 and WbCol-4).