

# Malaria vector based VIMTs: challenges and future

## Abstract

Malaria, AIDS and tuberculosis are considered as the important infectious diseases in the world. Malaria has a close relationship with the climate and life style of the human. Therefore, malaria is known as the disease of the poor countries. With regards to its importance, WHO invited scientists with different specialties for programming the second global malaria eradication program? The recommendation of the vaccine consultative group was development of the vaccines that interrupt malaria transmission (VIMTs). VIMTs are composed of different type of vaccines which vector based TBVs are one of them. Vector based TBVs have advantages in compare other type VIMTs such as impact on the parasite life cycle and mosquito fitness simultaneously. Therefore, targeting the vector and parasite antigens simultaneously can be considered as a robust tool to reach the aim of global malaria eradication program.

**Keywords:** malaria, vaccines that interrupt malaria transmission, transmission blocking vaccine, vector borne diseases

**Abbreviations:** TBVs, transmission blocking vaccines; VIMTs, vaccines that interrupt malaria transmission; WHO, world health organization; malEra, malaria eradication program

## Introduction

In the modern world, with regards to the improvements in human life style and breakthroughs in medical sciences, vector-borne diseases such as malaria are still as public health challenge worldwide.<sup>1</sup> The most important reason is related to the movement capability of the vectors. Therefore, pathogens can be transported throughout the world.<sup>2</sup> Malaria is caused by protozoan parasites of the genus *Plasmodium* and transmitted to humans through the infected female *Anopheles* mosquito's bites.<sup>3,4</sup> According to the WHO malaria report, in 2013, it has been estimated that 3.3billion people are at risk of malaria infection and 1.2billion are at high risk for this malignant malady. Furthermore, there were an estimated 584 000 out of 198million cases of malaria happened entire of world led to deaths in 2013. In addition, malaria is the cause of more than 430 000 child's deaths in Africa annually.<sup>5,6</sup>

These undesirable statistics make that malaria be on the focus of international considerations to develop a comprehensive agenda for its control and global eradication. The first malaria eradication program was broken down for many reasons which the ignorance of the scientific comments and the lack of knowledge about endemic regions were the important factors.

With regards to the importance of malaria and its social and economic effects, in October 2007, the Bill and Melinda Gates Foundation summoned the Malaria Forum with cooperation with WHO and the Roll Back Malaria (RBM) for the second global malaria eradication program. More than 250 scientists were attended in 20 consultative meetings and published their solutions in different aspects such as drugs, vector control, modeling, etc.<sup>1</sup>

Vaccine consultative group was introduced a new concept with the broad scope: Vaccines that Interrupt Malaria Transmission (VIMTs). They emphasized that VIMT's development is very necessary for endemic regions that have passed the pre-elimination and are toward to the eradication step.<sup>7</sup>

VIMTs can be included one or more of these types of malaria vaccines: classical Transmission Blocking Vaccines (TBVs), pre-

erythrocytic vaccines, erythrocytic vaccines and vector based vaccines. Most of the malaria vaccines which have been studied or those that are in clinical trials are related to parasite antigens. But, few studies have been performed that their targets are vector based antigens which are important in the sexual parasite development. The performed studies have showed that there are vector based cofactors which those are important in providing the parasite nutritional requirements or bio-barrier transferring.<sup>8-20</sup>

Targeting the vector based antigens has some advantages in compare to parasite based TBVs which the most important of them are:

- I. Vector based antigens are usually conserved proteins which are very important for mosquito surviving and those have very similar structure and function in different species.<sup>12,14,21</sup> Therefore, raised antibodies against a conserved protein of one species can be effective against the similar one in other species and if you find an antigen with these specifications, you can design and develop a universal TBV which is effective against different vectors with distinct geographical distribution.
- II. Targeting the vector antigens may be affect the longevity and fecundity of mosquitoes. For example, lavazec et al.,<sup>16</sup> reported that anti-CPBAG1 antibodies are reduced the number of *An. gambiae* eggs in compare to control groups. Therefore, affecting the mosquito fitness and population size can improve the impact of vaccination.<sup>16</sup>
- III. One of the problems of selecting the plasmodium antigens is antigenic variation due to the pressure of immune system.<sup>22-24</sup> But, this problem will not be happened in the case of mosquito antigens.
- IV. With regards to the benefits of vector based TBVs, but there are some challenging items for these types of TBVs as well. Because the human immune system is naturally not boosted against mosquito antigens, the selected antigens should be high immunogenic, robust adjuvants should be used for vaccination or revaccination should be considered periodically.<sup>11,25</sup> Furthermore, if targeting the vector based antigens affects the mosquito fitness,<sup>16</sup> it will result to the increase of resistance population. Therefore, before application of these types of vaccines, well characterization and evaluation should be performed. Combination of more than one antigen can be reduced this effect as well.

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## Conclusion

With regards to the importance of malaria disease, WHO global malaria eradication program and malEra guidelines to reach the global eradication, development of the VIMTs is one of the necessities in this path. According to the specifications of the vector based VIMTs and the important role of the mosquitoes in malaria infection, these types of vaccines can be considered as an effective tool to reach and keep global eradication.<sup>26</sup>

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## Conflicts of interest

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