

## Editorial

# Varicella-Zoster Virus Clades and Vaccination Program

**Elena Bozzola<sup>1\*</sup> and Mauro Bozzola<sup>2</sup>**

<sup>1</sup>University/Hospital Department of Pediatrics, Pediatric and Infectious Diseases Unit, Bambino Gesù Children's Hospital, IRCCS, Rome, Italy

<sup>2</sup>Internal Medicine and Therapeutics Department, Pediatrics and Adolescentology Unit, University of Pavia, Fondazione IRCCS, San Matteo, Italy

\***Corresponding author:** Elena Bozzola, Pediatric and Infectious Diseases Unit, Bambino Gesù Children's Hospital, IRCCS, Piazza Sant'Onofrio, Rome, Italy

**Received:** March 07, 2016; **Accepted:** March 07, 2016;

**Published:** March 09, 2016

## Keywords

Varicella-zoster virus; Clade; Vaccine

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Varicella-Zoster Virus (VZV) is a world-wide distributed pathogen responsible of varicella and herpes zoster. As both diseases may result in significant morbidity and economic burden, the implementation of routine varicella vaccination programs should be advised [1].

Varicella vaccines currently used in immunization schedule derive from a Japanese Varicella-Zoster Virus (VZV) wild-type strain isolated from a child with typical varicella named Oka (parental Oka, pOka). While pOka is virulent in vivo, the attenuated Oka Vaccine Virus (vOka) is an avirulent virus that is able to provide protection from varicella-zoster disease [2]. Currently, one dose of varicella vaccine is thought to be moderately effective in preventing varicella diseases (81%) and highly effective in preventing moderate and severe manifestations of varicella (98%). Moreover, a second dose is able to increase protection against varicella disease up to 92% [3].

Molecular epidemiological studies have been performed to investigate and monitor the genetic variability and phylogenetic relationship of VZV strains throughout the world. In early studies, VZV DNA was characterized using single nucleotide polymorphism based analysis of the VZV genome, which demonstrated inter-strain variations among wild-type isolates as well as differences between wild- and vaccine-type viruses. Consequently, VZV genotypes, based on geographical localization of the isolates, were proposed [4].

With the beginning of the 21<sup>st</sup> century, and the availability of the full genomic sequencing, there was a significant rise in the number of available VZV full-genome sequences which are essential for the definition of different VZV clades. To date, it is well established that VZV can be divided into five major clades (1 to 5), confirmed by full-genome sequencing. In addition, four novel clades (6 to 9) have been proposed but they still need to be confirmed by further complete sequences [5-7]. Additionally, several studies have demonstrated a regional dominance of specific VZV clades, most likely in dependence on environmental factors, evolutionary conditions and host-virus interactions and/or importation of viral strains. Several studies were

performed in Europe to identify the circulating VZV clades. On the basis of these studies, clades 1 and 3 strains have been reported mainly in Europe and in America. As for clade 2 strains, they have been frequently detected in Asia. Reports referring to clades 5 and 6 strains generally pertain African regions. In details, in European countries 50% strains were typed as clade 1 strains and 37% strains were typed as clade 3 strains [8]. Within Europe, clade 6 strains were also found frequently in France (10%) and Italy (11%). In details, clade 6 strains were more commonly detected than clade 3 strains in Southern Europe [9]. The higher frequency of clade 6 strain might be explained by the migration of persons with African origin.

As well as for Europe, clades 1 and 3 represent dominant clades of the circulating VZV strains in the USA, Canada and Mexico. Presence of clades 5 strains in America was compatible with the immigration of people with African origin. Clade 2 represents the dominant one in Asia, except for the Indian subcontinent, which comprises India, Bangladesh and Nepal. In fact, clade 2 strains were found not to circulate in India, Nepal and Bangladesh whereas clades 4 and 5 strains were dominant. Finally, as for Thailand, just clade 3 strains had been detected, probably as they were imported into the native population by immigrants coming from European countries [8,10].

Genotypic surveillance may be helpful for understanding VZV circulation, for identifying new mutations and for implementing vaccination strategies.

The occurrence of "vaccine escape" genotypes of varicella is a key question in immunized breakthrough cases with little information available on the distribution of varicella genotypes and their relationship to virulence. A strictly genotyping control of circulating clades may increase the likelihood of identifying genotypes associated with more severe disease or affecting immunocompromised patients, such as those with a history of underlying malignancy, steroid use or immunosuppressive therapy, HIV infection, or solid organ transplantation. Finding which genotypes are more frequent among patients hospitalized for VZV complications may also lead to establish links between sequence variations and virus pathogenicity [11]. In particular, the possibility of recombination between wild-type and vaccine strains should be considered after entering of varicella vaccine strains, clustering into clade 2, into countries where the routine varicella vaccination is currently used.

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