Antigen specific VZV reactive t cells – one-size-fits-all?

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Background

Infections caused by the varicella-zoster virus (VZV) are typically believed to be a pediatric disease (Chickenpox). After primary infection, VZV is remaining dormant in human ganglia until reactivation decades after the initial infection. The resulting Herpes zoster is mostly characterized by painful skin rash but also can affect other organs and may cause lethal complications. Due to this complex disease pattern, a broad spectrum immune monitoring beyond serological standards is needed.

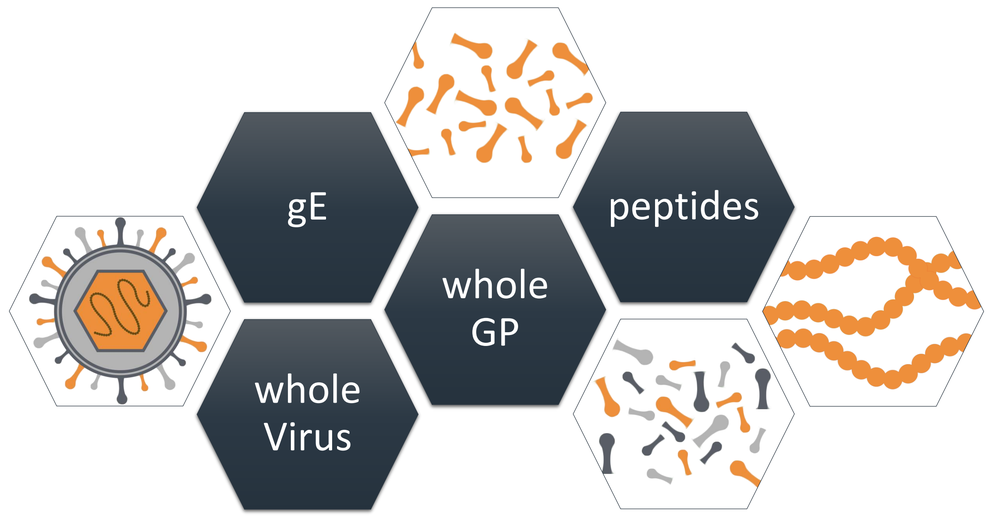

Fig. 1: Schematic overview of the different tested VZV antigen types. VZV whole virus lysate, whole native glycoproteins, recombinant glycoprotein E (gE) and synthetic peptides specific for lytic and latent immune response

Objectives

With this proof-of-concept study we show various pattern of t-cell immune reactions against different types of VZV antigens depending on the age and vaccination status of healthy donors (HD).

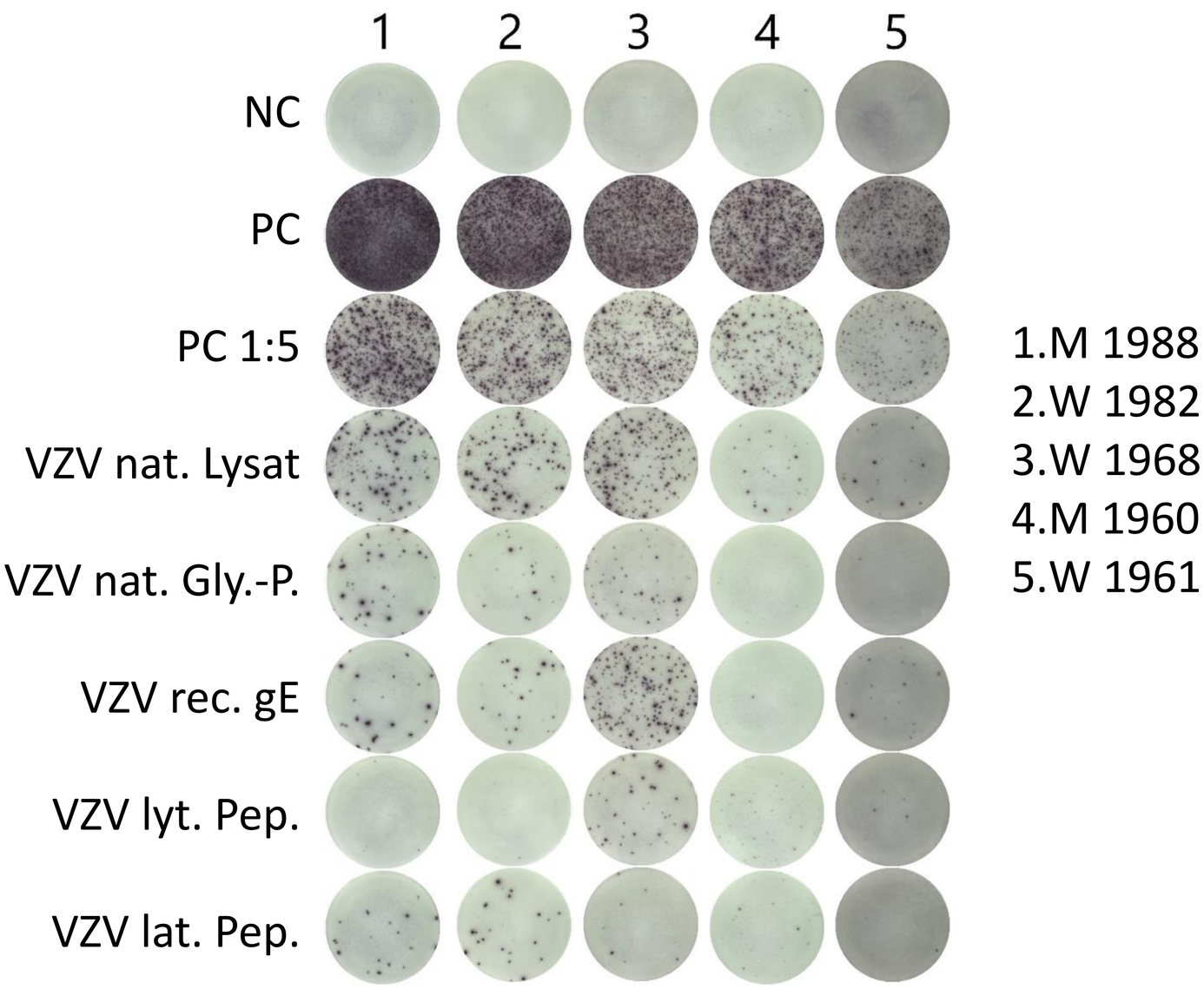

Fig.2: Representative pictures of various health donors stimulated with different types of Varizella zoster antigens. HD younger than 50 years (1. and 2.) are showing a strong immune reaction to all of the tested antigens expect the synthetic peptides specific for the lytic immune response. After vaccination (3.) a strong immune reaction against the recombinant gE and peptides specific for lytic immune response could be detected. In samples from donors older than 60 years (4. and 5.) the number of VZV reactive t cells decreases dramatically. In this samples mainly a weak reaction against the whole virus lysate could be observed.

Conclusion

Notwithstanding the small sample size of this study, clear age related differences can be observed. We conclude that VZV whole virus lysate and whole native glycoproteins are unsuitable for the measurement of immune response during or after viral reactivation in adolescent patients. For the determination of pathological changes in immune state, synthetic peptides are mandatory. On the other hand, VZV whole virus lysate may be used as an indicator to find the accurate moment for vaccination in adults.

Methods

An EliSpot assay has been used for the detection of interferon gamma releasing t-cells after stimulation with VZV whole virus lysate, whole native glycoproteins, recombinant glycoprotein E (gE) and synthetic peptide pools specific for lytic and latent immune response.

Results

HD younger than 50 years are showing a strong immune reaction to all tested antigens expect the synthetic peptides specific for the lytic immune response. After vaccination, a strong immune reaction against the recombinant gE and peptides specific for lytic immune response could be detected. In samples from unvaccinated donors older than 60 years the number of VZV reactive t-cells decreases dramatically. In this samples mainly a weak reaction against the whole virus lysate could be observed.

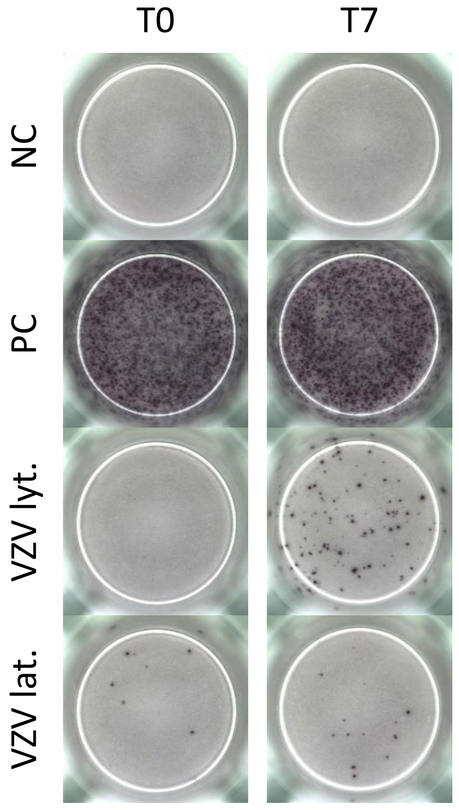

Fig.3: Representative pictures of a previously VZV infected donor before and seven days after vaccination. PBMCs have been isolated from a donor naturally infected with chickenpox during childhood before and seven days after vaccination with Shingrix, GlaxoSmithKline Biologicals SA. Cells where stimulated with the AID VZV Lytic-Mix (VZV lyt.) and VZV Latent-Mix (VZV lat.) peptide pools and analysed in the Interferon gamma EliSpot assay. Shingrix as well as the AID VZV Lytic-Mix are based on glycoprotein E (gE). After vaccination a strong t-cell response against VZV can be detected via the secretion of Interferon gamma. The t-cell reaction against the latent antigen mix remains unchanged. The negative and positive control wells are shown for visualization of correct EliSpot assay performance and to ensure a sufficient number of stimulatable t-cells (NC: negative control, cells in media only; PC: positive control, PWM (Pokeweed mitogen) stimulated cells). For a better visualisation of results an enzymatic Interferon gamma EliSpot has been chosen.

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