Antigen specific VZV reactive t cells – one-size-fits-all? Effect of the antigen type depending on the question

Ettischer-Schmid N. [1], Strecker K.[1], Preyer R. [1]
[1]GenID GmbH, EliSpot, Strassberg, Germany

Introduction

Infections caused by varicella-zoster virus (VZV) are typically pediatric diseases (Chickenpox). After primary infection, VZV is remaining dormant in human ganglia until reactivation decades after the initial infection. The resulting Herpes zoster is 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 standard analysis is needed.

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).

Methods and results

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

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

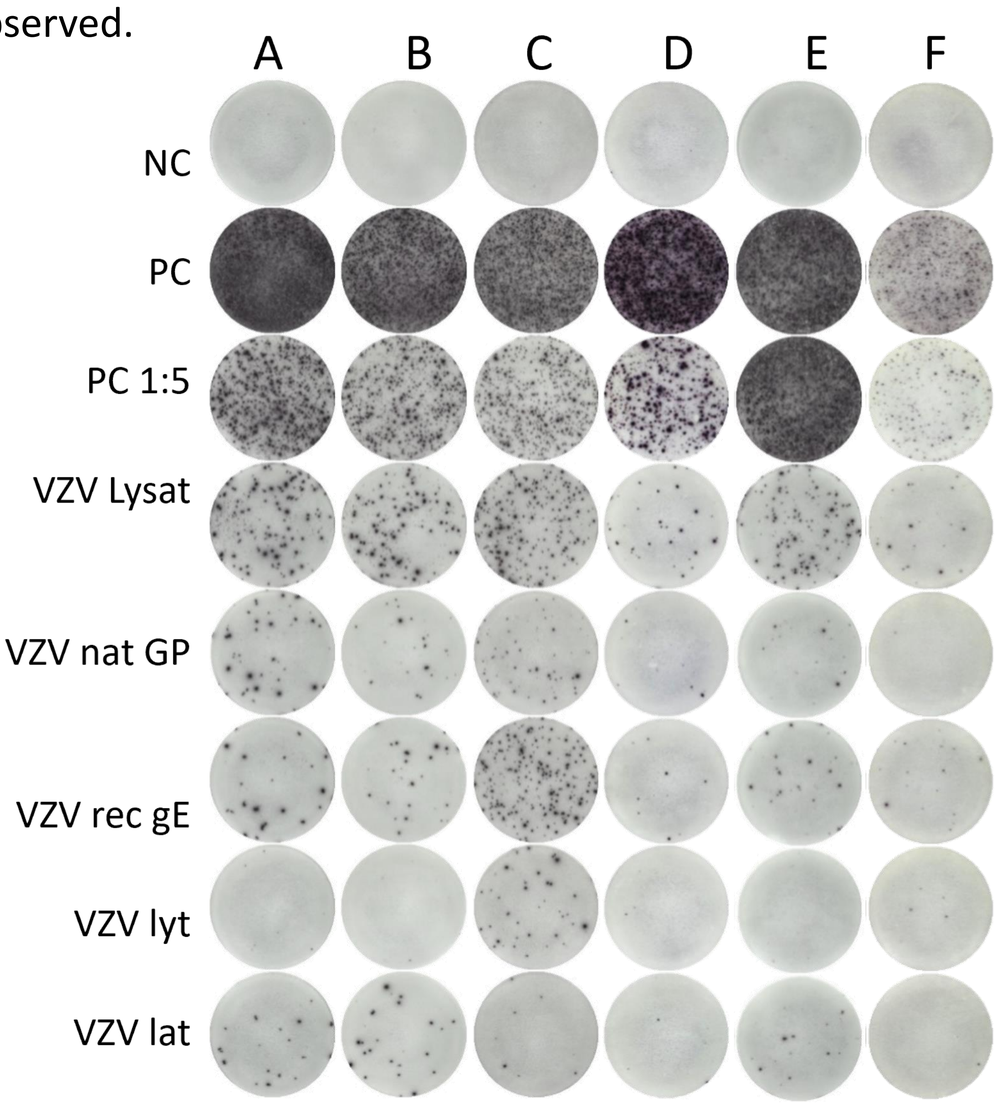

Fig.1: Representative pictures of a VZV vaccinated and unvaccinated donors

PBMCs have been isolated from a donor 18 months after vaccination with Shingrix, GlaxoSmithKline Biologicals SA and 5 non-vaccinated donors with or without known history of VZV in childhood.

Cells were stimulated with the AID VZV Lytic-Mix (VZV lyt) and VZV Latent-Mix (VZV lat) peptide pools, VZV Lysate, native Glycoproteins (native GP) and VZV recombinant gE (rec gE) and analysed in the Interferon gamma enzymatic assay. Shingrix as well as the AID VZV Lytic-Mix are based on glycoprotein E (gE). 18 months after vaccination still a strong T cell response against VZV can be detected via the secretion of Interferon gamma. Shown is the IFNy secretion.

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).

(A)M 1988 no vaccination, VZV in childhood (B)W no vaccination (C)W 1968 vacciantion 2020/2021 (D)W 1983 no vacciantion (E) W 1982 no vaccination, VZV in childhood (F)W 1961 no vaccination no record of VZV

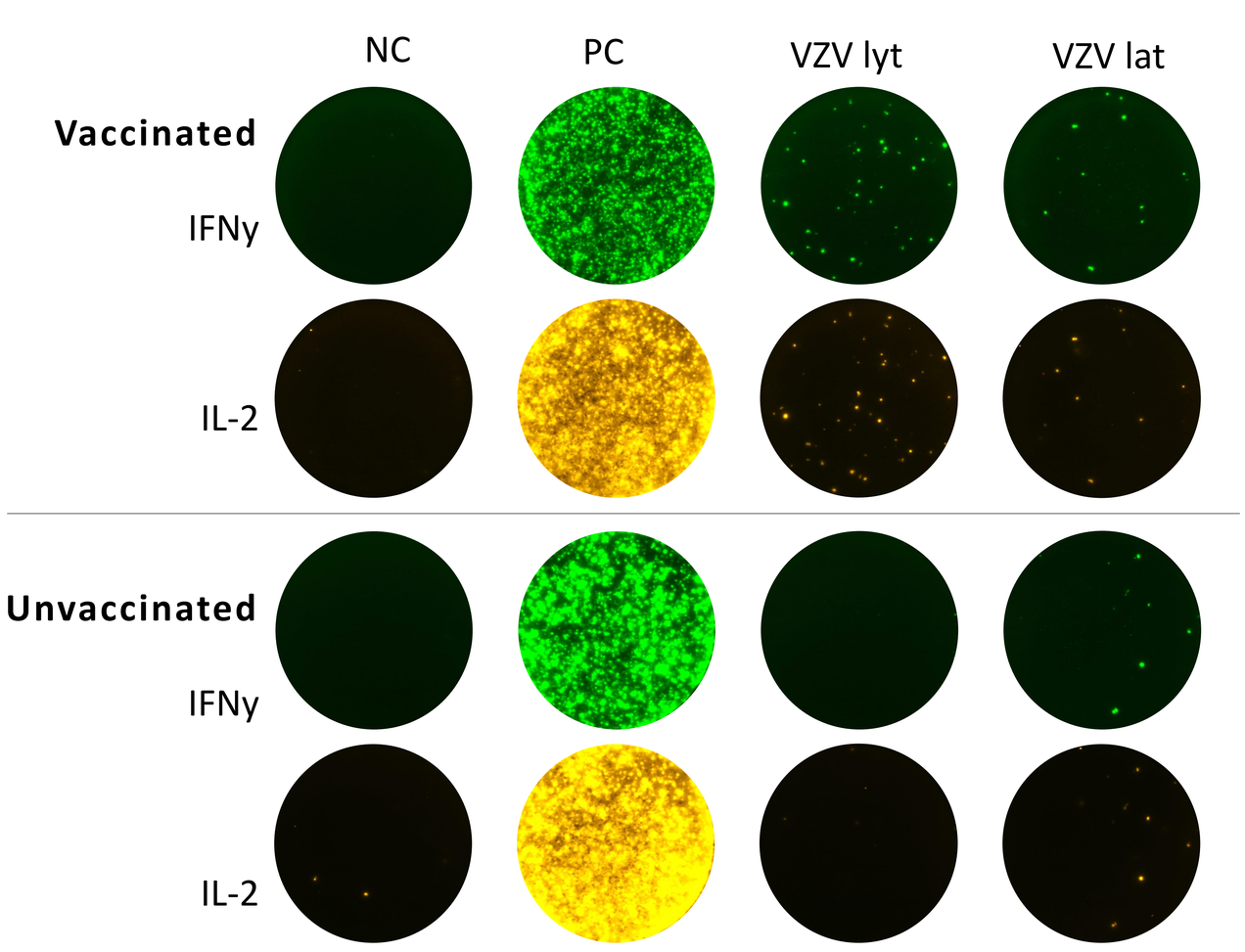

Fig.2: Representative pictures of a 2 colour fluorescent EliSpot (*i*Spot) from a non-vaccinated and a vaccinated donor in comparison.

PBMCs were analysed with the AID IFN-y / IL-2 (Interleukin-2, memory T cell) *i*Spot and stimulated with the VZV Latent and Lytic-Mix peptide pool.

18 months after vaccination still a strong T cell response against VZV can be detected via the secretion of Interferon gamma and IL-2 (memory t cells). Shown is the IFNy secretion (A; green channel) representing activated T cells, the IL-2 secretion (B; red channel) of memory T cells.

In contrast, the unvaccinated donor shows only few T cells reacting with latent peptides and no reactive T cells for lytic peptides.

Conclusion

Notwithstanding the small sample size of this study, clear age-related differences can be observed. We conclude that VZV lysate and native glycoproteins are unsuitable for the measurement of immune-response during or after reactivation in adolescent patients. For the determination of pathological changes in immune state, synthetic peptides are mandatory.

Regardless, VZV lysate may be used as indicator to find the accurate moment for vaccination in adults.

AID Autoimmun Diagnostika GmbH
D-72479 Strassberg

Tel. +49 (0)7434 9364-0
Fax +49 (0)7434 9364-40
info@aid-diagnostika.com

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