[Short Communication] Measles: 1963-2023, Immunology of a Morbillivirus

Brent Brown

Funding: No specific funding was received for this work.

Potential competing interests: No potential competing interests to declare.

Abstract

Measles is a virus, abbreviated to MeV, that has long been known to be causal in infant disease and affect infant mortality, remaining a public health issue of priority. The causal virion is defined biologically within the Family *Paraxmyxoviridae*, Genus *Morbillivirus* and Species *MeaslesMorbillivirus.* Similar to other viral infections, MeV is an airborne infection with the virion particle composed of a negative (-ve) sense single-stranded (ss) ribonucleic acid (RNA) genome code, around 15-16kb in size, encoding for eight predominant proteins. The first isolation of MeV occurred in 1954, known as the “Edmonston strain”. A team at Boston Children’s Hospital comprised of John Franklin Enders and others who isolated MeV from a 13-year-old serum sample. Alongside Samuel Katz and notably Maurice Hilleman, this led to the development of the first live attenuated vaccine, when in 1971, the first trivalent mumps, measles and rubella (MMR) vaccine was licensed for use in immunisation programmes in the United States of America (USA). Shortly after, in 1980, the eradication of Smallpox was confirmed by the World Health Organisation (WHO), which had been the predominant debilitating pathogen of the 20th century. Measles was then considered to be the cause of 2.6 million deaths each year. Around 1986, the MeV haemagglutinin (H) protein was crystallised *in vitro*. The introduction of MMR immunisation previously and after reduced mortality to around 110,000 annually. The rates of MeV disease since 2017 have been rising of a pathogen that is largely preventable through immunisation programs that evoke immune system responses. Smallpox (VARV) and the Rinderpest virus (RPV), a member of the same

Morbillivirus genus as MeV, remain the only other animal pathogens eradicated. The lack of antigenic variation of the MeV is suggestive that MeV remains the third pathogen to potentially be eradicated. Here is a discussion of contextual Measles immunological characteristics to elucidate this further.

Brent Brown*

Independent Immunopharmacologist, C/O Biochem123 Education, London, UK, www.biochem123.org

***Correspondence:**

Brent Brown, London, UK: info@biochem123.org

ORCID iD: 0000-0001-5238-6943

Keywords: Adaptive, Measles, Immunology, Innate, Pathogenesis.

Introduction

Comparatively, less is known about the immunological aspects of MeV natural innate and adaptive immune responses due to therapeutic immunisation utilised largely since 1963. A clear prophylactic benefit has since been observed at the same time as technological advancements, including genomic sequencing and DNA discovery, together with the discovery by Kohler and Milstein in 1975 of how to produce monoclonal antibodies that may lead to further global disease reduction of other pathologies. However, here we discuss what is known so far as *Paramyxoviridae* can cause severe disease, including blindness and brain damage [1][2][3]

Measles virus (MeV) immunisation is considered to induce long-term immunity; however, little is known about the underlying mechanisms so far [4]. The first cloning of a full-length infectious measles virion occurred around 1995 in Zurich, at the Pasteur Institute, routinely utilised commercially in preparations as an attenuated vaccine under approval by a variety of organisations (see Supplementary Materials). The MeV virion is also comparatively considered to be a potential viral vector that can be adapted to target many other viral pathogens like Human Immunodeficiency virus (HIV), Dengue Fever virus (DENV) and Chikungunya virus (CHIK). In addition, MeV further has potential applications as an oncolytic viral (OV) vector, for example, recently examined as a potential therapeutic in 2022 in treatment for glioblastoma [5][6][7][8]. The methodology behind this is long known through active immune response induction causal of long-term immunogenic host responses and immunity to reinfection, indicated by the near eradication of this pathogen [9][10]. Measles remains apart as a virulent pathogen from many other viral infections because of the overall R0 (transmission rate), which is considered to be higher than many other pathogens. The R0 is indicated within the range 12-18 with affliction in vulnerable infant populations predominantly [11]. Efficacy and safety of MMR immunisation were the subjects of debate in the early 21st century; however, seminal reports in late 2021 utilising population real-world data

(RWD) were suggestive of an efficacy of 95% after 1 dose and 96% after 2 doses to either the trivalent or quadrivalent options that were subsequently manufactured and designed to counter Varicella Zoster (VZV) virus viral antigen epitopes [12].

Given the prior reduction in overall MeV mortality, immunisation against MeV, therefore, has nearly led to the global eradication of the third virus and may still do so. The terminology of vaccination and immunisation are derived from research of the original vaccinia virus (VV) and Smallpox (VARV) strains training and evoking active immunological responses in a host animal or human. Active immunity is commonly used to describe the process of exposing a host to an antigen and can be natural or acquired; similarly, passive immunity can also be either natural or acquired [13]. The two terms are historically used to differentiate between the two types of host immune responses, with the first utilised that may be long-lasting following infection or immunisation. The second passive type of immunity refers to the transfer of antibody types in hosts, for example, Immunoglobulin G or similar other licensed preparations like Human Rabies Immunoglobulin (HRIG) or other monoclonal antibody preparations (see Supplementary materials)

Different vaccine vectors utilised can be a beneficial factor in the immune system programme to prime both B and T cells, training the innate and adaptive immune system response. Many phenotypes of immune cells are now known in the 21st century. Longevity and kinetics of antibody production by B cells require T cells to adequately stimulate a recall memory response. Furthermore, the subtypes of B cell antibodies were described further in the 21st century alongside other T cell phenotypes (e.g., T_{REGS} and T_H17 cells). Below is presented the immune cell detail known so far about immunological correlates and phenotypes that pertain to a host human response to natural MeV infection.

Structure of Measles Virus

The MeV virion particle size is 15,894kb from the 3’ end of the -ssRNA strand. This encodes a nucleoprotein (N), haemagglutinin (H), with a trimer C/P/V, matrix (M), and fusion (F) protein together with a polymerase (L) enzyme towards the 5’ end of the RNA genome. The L protein polymerase sequentially transcribes by binding to the MeV RNA at the 3’ leader, with polyadenylation occurring during synthesis with V protein produced through RNA editing and a P protein produced from the C protein. Viral attachment of the MeV virion particle can occur through the haemagglutinin (H) protein attaching to the host cell receptor with the fusion (F) protein, allowing entry through the plasma membrane (PM) where the viral mRNA is capped and polyadenylated within cellular cytoplasm [14]. Much remains unknown about how measles transverses cells and replicates intracellularly; however, it is indicated that the MeV virion particle forms inclusion bodies (IBs) without a membrane, rich in three MeV synthesised proteins that are N, P, and L proteins [15].

History of Measles

Genetic characterisation of the measles virus indicates ancestry around 1915, with extensive research indicating that the H protein was comparatively conserved, explaining why current therapeutics remain comparatively successful in the prophylaxis of MeV infection [16]. Mutation rates of the MeV particle were estimated in 1999 at 9 x 10^5 per base/replication

with a genomic mutation rate of 1.43 per replication cycle, indicating that point mutations were comparable between other -ssRNA viruses, including poliovirus but also vesicular stomatitis virus (VSV) conferring resistance to monoclonal antibodies then [17].

More recently, in 2015, investigations occurred in Canada of specific MeV H1 and D8 strains[18]. Previously, 24 known genotypes had been sequenced. Indeed, in 2018, the MeV genotypes in global circulation decreased to 4 in 2018. These were denoted by two MeV strains (B3/D8) together with two others (D4/H1) globally during 2020 [19]. Out of these, two (B3/D8) are known to be endemic across six of the WHO regions [20].

Development of Measles Research

Many viral protein point mutations can affect immunologically programmed responses to pathogens. During 2009, as monoclonal research development continued, it could be seen that the MeV particle utilised one predominant receptor discovered in 1993 (CD46) that could be predominantly blocked by either polyclonal or monoclonal antibodies akin to a pharmacological antagonist preventing cellular infection similarly to immunisation evoking an immune response [21].

Since then, protein epitope prediction and molecular mapping have remained an ongoing development for the immune system to be trained to be more effective in responding. During a host immune response to pathogenic antigens (epitope peptide), fragments are presented and processed through type two types of Major Histocompatibility Complex (MHC type I/II) utilising antigen-presenting cells (APCs) including dendritic cells (DCs), monocytes and macrophages amongst a network of better-characterised immune system cells [1][2][3]

Measles Receptor-Mediated Infection

Measles cellular infection was initially considered to occur through one receptor (CD46). In 2000, MeV eradication was indicated in the USA and remained a target by the WHO for eradication, with sporadic outbreaks occurring since. It is considered through research that MeV infects white blood cells (WBCs) called lymphocytes expressing a second receptor (CD150) known as a signalling lymphocyte activation molecule family member 1 (SLAMF1) utilising nectin-4 as a host cell receptor, with these specifically expressed on certain subtypes of cells including DCs [22][23][24].

CD46 is considered to be an adhesive entry receptor that MeV utilises for cellular entry characterised before 2000. The first protein receptor CD46 that MeV utilised to enter the host cells was found to be activated and expressed within the myeloid cellular lineages and could also bind to complement proteins (C3b/C4b), a crucial part of coagulation pathways. Antibodies synthesised by B cells possess two antigen binding domains that recognise pathogenic epitopes (Fab) receptors and constant (Fc) protein domains. These affect antibody opsonisation (binding) to cellular membrane receptors to affect an immune response through signalling and homeostatic complement regulation utilising fibroblast growth factors (FGF) as well as angiogenic factors contributing to vascular growth. Knowledge of this then was less unknown; however, the CD46 receptor utilises is also indicated to be preferentially expressed during oncogenic disorders and is described as

a “pathogen magnet” in differential infections [21][25]. It appears that the initial receptor, CD46, is localised with many proteins that can enhance fibroblast growth factors necessary during common skin and systemic viral infections affecting different organ systems.

The second receptor method utilised for cellular infection, CD150, is considered to be expressed throughout the primary immune system organs (bone marrow/thymus), secondary (spleen, tonsils, lymph nodes), as well as tertiary (e.g., bronchus-associated lymphoid tissue (BALT) as well as on platelets and haematopoietic stem cells (HPSC).

Nectin-4 (PVRL4) has also been indicated as a third receptor of relevance during MeV infection, overexpressed in specific tumour carcinomas like breast, lung, colorectal, pancreatic, as well as ovarian cancer, usually expressed at lower levels during infancy when MeV infection frequently occurs [23][24]. Nectin-4 clarification came as recently as 2012, similar to other types of poliovirus receptors (PVR) documented prior, like CD155 [26]. These are individually considered as nectin-1 (CD111), an entry factor receptor for herpes simplex (HSV-1/HSV-2), with Nectin-2 (CD112), an entry factor of human herpes viruses (HHV), whilst Nectin-3 (CD113) was also characterised prior.

Reduction in lymphocyte counts can occur (lymphopenia) through excessive apoptosis (cell death/proliferation) in many disorders, where the regulatory homeostatic immune system is imbalanced through host cell receptor viral entry and cytokine regulation. However, recently, chemokines also can affect the checkpoint balancing immune cell signalling in an autocrine/paracrine fashion similar to other hormones. Measles particle virions appear to disturb this normal homeostatic cellular function in natural infection outlined further below, with much remaining unknown.

Innate Immune Responses During Measles Infection

Early indicators in 2001 appeared examining natural MeV infection, as duration and kinetics since MMR immunisation remain largely unknown. Kinetics of the immune response indicate that during natural infection by MeV, two specific antibody types, defined as immunoglobulin proteins, IgM and IgG, are synthesised at 11 days after infection, peaking at 17-24 days for IgG in non-human primates (NHP) *in vivo* [27]. However, there are at least 4 relevant subtypes of IgG (IgG1, IgG2, IgG3, IgG4) as well as 2 subtypes of IgA (IgA1, IgA2) alongside IgE and IgD with others like IgY in avian species. Nevertheless, it was then shown that one type of IgG, IgG1, is predominant in sera early after MeV infection, whilst IgG2/IgG3 appear at cyclical levels during cellular memory and isotype switching with IgG4 appearing later after MeV infection [28]. Population serology studies in 2020 (n=1092) examined neutralising antibodies (nAbs) between 10-12 years after either infection or immunisation against MeV [29][30]. Decreases in measles mortality occurred over 30 years prior when much of this remained unknown and still does. It was also indicated that the other antibody type (IgM) detected was considered crucial in reducing host viral propagation, host immune response, and time of sample collection, as well as being the second key antibody type alongside IgG for diagnostic assays [28]. However, other research indicates 4 years after MeV infection that IgG2 and an unknown antibody subtype of IgG2 are also relevant during convalescence to natural MeV infection, with IgG1 and IgG3 remaining the dominant earlier humoral antibodies produced [31]. These were interesting observations because, *in vivo,* mice rather than humans are observed to have a further 3 subtypes of

IgG2 [32][33][34]. Many factors affect the rate of antibody generation and persistence, but memory T cell responses play a large role in influencing the innate immune system. Since MeV immunisation and global disease reduction, technological evolution and genetic sequencing have further discovered other protein factors in the immune system. These include cytokines and chemokines like type I interferon (IFN), type II IFN, or type III IFN discovered between 1957 and 2003 alongside a host of Pattern Recognition Receptors (PRR) like Toll-like receptors (TLR), amongst others.

Immunisation against MeV traditionally occurs in two doses in infants, providing a known therapeutic benefit by training the immune system to recognise the MeV viral pathogen epitope presented to T cells. This therapeutic benefit of immunisation may extend beyond utilising MeV infection as a potential oncolytic virus depending on shared epitopes presented by the virus in common with other viral or bacterial pathogens [35].

Researchers in Boston, in a crucial study, observed in serological analysis (n=77) that during natural MeV infection, the antibody repertoire was reduced by up to 73% during MeV natural infection in children [36]. Concurrent observations were that the MeV epitope repertoire presented to the immune system during infection can be suppressed in non-human primates (NHP) *in vivo* (n=4). Therefore, this apparent dampening or suppression of the immune response caused by MeV may affect the human host's immune response to an array of pathogens, including Herpesvirus, Papillomavirus amongst many other bacterial infections (e.g., *Streptococci*) for up to 5 months after natural infection[35]

During the acute phase of MeV infection, circulating B cells, as well as T cells, are infected through MeV adhesion to at least one receptor (CD46). Receptors are present throughout the lymphoid tissues, germinal centres (GCs) and draining lymph nodes (dLNs). On the other hand, MeV infection is associated with a robust immune response to MMR immunisation, whilst infection is indicative of B and/or T cell temporal lack of memory cell response remaining unclear.

Adaptive Innate Immune Responses during Natural Measles Infection

In 2012, reports emerged investigating to show both B and T cells could be infected by MeV[27]. The effector host response to MeV infection relies on at least two types of T cells. For example, effector memory (T_{EM}) cells but also recall of other helper T cell and cytotoxic T cell (T_H/T_C) responses to provide longer-term adaptive immunity. Other T cells include and are defined phenotypically as naïve (T_N) and regulatory T cells (T_{REGS}), whilst others secrete cytokines like IL-17 (T_H17 cells) amongst more T cell phenotypes. T cells that are infected by MeV include memory T lymphocytes lacking expression of receptor proteins like CD molecule proteins ($CD45RA^-$) or expressing other CD proteins ($CD45R0^+$) [37]. These specific T cells traverse and diffuse through endothelial cell layers (ECs), as well as within lymphoid tissues (bone marrow/thymus) and dLNs utilising leukocyte-specific adhesion molecules like CD62 ligands (CD62L).

It was noted that two types of T cells were preferentially infected, T_{CM} and T_{EM}, with the hypothesis that natural MeV infection induces immune cell temporal amnesia [2][27]. However, other types of cells that develop into B cells were observed as proliferating within LNs (follicular B cells) measured by Ki67, a cellular marker of proliferation. Suggestions were that apoptosis did not occur as measured by caspase-3 expression within T cells, but rather that MeV-infected cells

were preferentially killed by T_C cells producing an array of effector enzymes like perforins and granzymes.

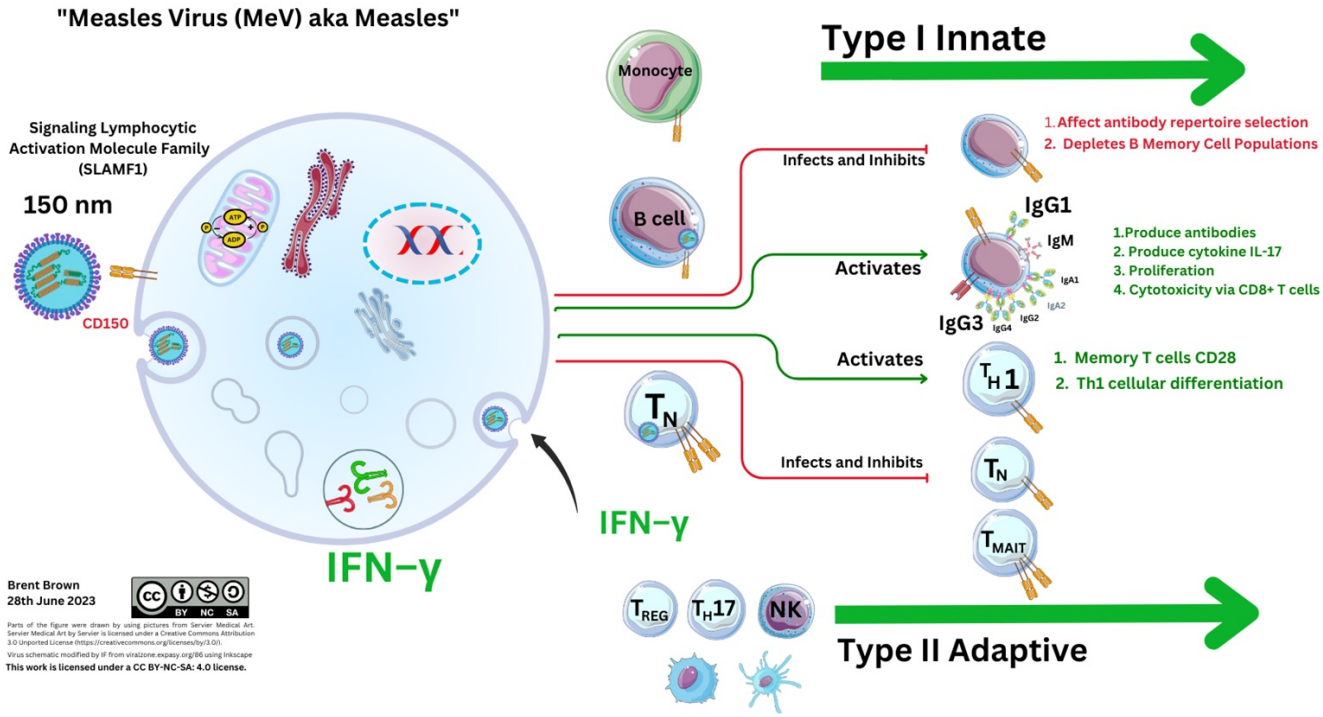

Figure 1. Measles Infection of Immune Cells

Other Cellular Adaptive Innate Immune Responses during Natural Measles Infection

Comparatively, less is known about the role of Natural Killer (NK) cells during MeV infection or other immune cell phenotypes in prior reviews. However, since the 1954 isolation of MeV, many of the T cell phenotypes are further defined by the expression of chemokines (CXC/CCR) as well as respective ligands (CXCL) alongside CD cellular membrane proteins by T cells. These include T central memory (T_{CM}) (CD45RA–CCR7+), or effector memory (T_{EM}) cells (CD45RA–CCR7–), and naive B cells (IgD+CD27–), or memory B cells (IgD–CD27+), as well as other B cells (CD20+) expressing an antigen-presenting protein receptor, the type II major histocompatibility complex (MHC) receptor (HLA-DR) [2][27][38][39].

Recent diagnostics commonly used up to 5 days after infection are real-time polymerase chain reaction (rtPCR), whilst serology assays have been reviewed elsewhere available for MeV indicative of sensitivity of 90.6% but also 100% specificity to date [40]. More recent outbreaks of natural MeV infection (n=26) are indicative that T cell responses in other T cell subtypes are affected, as defined above. These are follicular T helper cells (T_{FH}), alongside at least four other key T cell phenotypes being T helper (T_H1 and T_H2), as well as T_{REGS}, with T_H17 cell reduction occurring [41].

During MeV natural infection, it was similarly observed that B memory (B_{MEM}) cells were reduced, which would usually develop and stimulate other cells to form antibody-secreting cells (ASCs). Therefore, with B_{MEM} cellular count reduction,

there was an accompanying reduction in antibody secretion of two predominant types within serum and mucosal compartments (IgG and IgA); interestingly, increases in other B cells known as transitional B cells were observed being bone marrow resident B cells. The measles virus, therefore, has been confirmed to selectively deplete naïve B cell development with signalling pathways largely unknown but potentially affecting the immune response to other pathogens [42].

Chemokine Expression during Natural Measles Infection

During 2011, as chemokine research evolved, the role of CXCL12 was investigated and considered to be affected that may potentially affect antigen-presenting cells. It was then postulated that *RUNX3,* a regulatory transcription factor, could regulate and maintain CD4 and CD14 expression, thereby affecting monocyte differentiation with individual angiogenic and immunosuppressive activity[43][44]. This chemokine, CXCL12, is known as a B cell developmental growth factor, also called stromal-derived factor 1α (SDF-1α).

Further reports emerged in 2016 using unbiased mRNA-sequencing technology indicating that immunisation against MeV elicited the production through cellular messenger RNA of three key proteins: CD93, IL6, and CXCL12 [45]. As mentioned above, CXCL12 protein synthesis was observed to be downregulated during MeV infection. Therefore, it is plausible that this represents a key pathway with which MeV infection can alter both monocyte lineages as well as T cell phenotypes during disease. Interestingly, CD93 is a C-type lectin transmembrane receptor affecting cell adhesion and phagocytosis by antigen-presenting cells. In addition, CD93 appears to have a central function discovered since it has a negative correlation to T_H1, NK cells, but also myeloid-derived suppressor (MDSC) and follicular T helper (T_{FH}) cells in cancer [46]. It was furthermore considered that blockade of CD93 could sensitise tumours to immune checkpoint therapy [46]. Whereas interleukin-6 is a well-characterised cytokine performing a role as a chemoattractant for neutrophils during pro-inflammatory immune responses, whilst CD93 is found expressed by a wide variety of cell lineages including myeloid, myeloid cells, haematopoietic stem cells (HSPCs), Natural Killer (NK) cells and platelets concurrently with neuronal, microglial and endothelial cells (ECs) [47]. It was further clarified that IL-2, along with tumour necrosis factor (TNF-α) and a type II interferon (IFN-γ), are required for effective innate host responses during MeV infection. Previous articles indicate that increases in levels of soluble IL-2R (CD25), a marker of regulatory T cells (T_{REGs}) only discovered in the 21st century, occurs with cyclical IL-17 changes produced by T_H17 cells and others [48]. This was unsurprising as TNF-α is usually expressed within epithelial cellular layers during infection to many viral infections, as with MeV, where skin rashes are characteristic.

In 2017, the T cell response was further analysed, indicative that CD4$^+$ T cells produce IFN-γ during the MeV infection rash period along with cytokines required for Mϕ maturation into either M1ϕ or M2ϕ phenotypes (IL-4, IL-10 and IL-13) [49]; whilst antibody production occurs in a T_H1 type response considered to be beneficial. However, other cytokines like IL-17 were synthesised and secreted up to 126 days after infection, whilst the other T cells that include T_{REGS} and T_H17 cellular actions have not yet been measured [49]. Interestingly, both cell types expressed RORγt (retinoic acid nuclear receptor) [50]. These were shortly after clarified to be specific for the MeV H and N proteins.

Development in 2020 indicated that a second chemokine, CXCL10, found in serum concentrations could be a correlate of severity during MeV infection [51]. These were interesting observations because the receptor for CXCL10 is CXCR3, expressed on many immune cells that include DCs in varying degrees that are required for antigen presentation. More recently, it was observed that MeV infects cytokeratin-positive epithelial cells in bronchial and appendix epithelia with disruption of alveolar and bronchial epithelial cells and multi-nucleated cells expressing CD11c characteristic of the dendritic cell population (DC) or the macrophage (Mϕ) cells expressing CD68 [52]. Further details remain unknown.

More recently, since 2021, it is apparent that MeV can modulate mitochondrial DNA (mtDNA) throughout the course of MeV infection in common with both +ssRNA and -ssRNA viruses whilst affecting the cyclic GMP-AMP synthase (cGAS) pathways that potentially stimulate each of the type I/II/III IFN secretion pathways required for immune responses [39][53][54]. Therefore, it could be apparent that MeV differential proteins could, in fact, modulate the IFN systemic response essential to antiviral innate/adaptive cellular reactions unknown so far.

This report would be indicative of the crucial importance of immunisation against MeV, which seemingly could share an abundance of epitopes with many other pathogens. As recently as 2021, other emerging reports further confirm that MeV infects recently characterised mucosal-associated invariant (MAIT) cells expressing $CD3^+$ with MR1 (Major histocompatibility complex class I-related gene protein (MR1), alongside invariant NK (iNKT) cells denoted by $CD3^+CD1d^+$ [55][56]. These were crucial because MR1 protein can bind to vitamin metabolites such as those produced during riboflavin synthesis (vitamin B2) during bacterial infection with others unknown [57][58][59][60]. Other T cell phenotypes are defined that include γδ T cells that could be a factor unknown so far, and others like Vγ9Vδ2 T cells may play a part in the developmental immune response [61].

Limitations

Above, some of the research will have included *in vivo / in vitro* research studies. Immunisation is subject to both regulatory and local authority jurisdiction for further guidance. Research studies are also subject to regulatory authorities and the GLP process.

Discussion

It is currently indicated that common complications of measles are acute encephalitis and sclerosing panencephalitis, which can occur 7-10 years after MeV infection, with the most recent mortality data in 2018 indicative of around 353,000 fatalities per annum [62]. This is likely to be much longer than 10 years observed through a clear reduction in overall measles case counts and disease burden since the introduction of immunisation [63][64]. Differential MeV measles antibody profiles were examined in China (n=2629) recently indicative of potential threshold at around 14.3 years with antibody concentrations around 200 mIU/ml [65]. However, T-cell responses are known to be variable by age, adding to the complexities [66]. The arbitrary scale of antibody responses is being compared globally with the complexity of variance in reagents used determined by the specificity and sensitivity of the monoclonal antibody [67]. The resultant inhibition by

MeV infection of the Janus kinase (JAK1) enzyme crucial to nuclear IFN signal transduction thereby modulates the type I IFN response required, in effect freezing the type I IFN pathway and IFN synthesis [68]. More recently, since type III IFN discovery in 2015, it could be observed *in vivo* that this lack of IFN response was also accompanied by a lack of type III IFN response and measured by lack of specific mRNA gene transcripts (*MX/ISG56*) usually leading to lack of translation of type I/III IFN protein expression [69]. In 2003, when type III IFN was discovered, it was indicated that the MeV C protein may suppress type I IFN (IFN-α or IFN-β) [54][70]. It was thus indicated that the timing of immunisation could affect the comparatively efficacious nAb response during MeV immunisation programmes, usually in infants under 4 years old [71]. Whilst CD150 was confirmed as the key MeV cellular entry receptor prior to 2018, it was noted that MeV seemingly infects T_N cells and B_{MEM} cells as well as both DCs and M1ϕ/M2ϕ but not the other key antigen-presenting cells that were monocytes *in vivo*. Research and laboratory research opinions vary on whether MeV infects monocytes; however, historically, this was observed in 1975 research [72][73]. It is possible that MeV appears causal in cytolytic activity in lymphocytes between acute and severe MEV infection [41]. Seemingly, MeV may cause selective immune cell amnesia, with the role of T_{REGS} and NK cells remaining unknown. However, one project in 1990 examined NK cell responses, which did appear unresponsive but could be rescued *in vitro* by the DC maturation/stimulation cytokine IL-12[74]. Cytolytic activity of *Paramyxoviridae* is known in similar viruses of this family[1]. Much remains unknown to this day.

Conclusions

The longevity of either humoral or adaptive correlates to MeV infection or vaccine correlates remains unknown currently, although longitudinal studies point towards a natural infection and immunisation against MeV inducing high concentrations of neutralising antibodies (nAb) that can be preventative of pathogenic diseases. Therefore, the relevance of MeV as an infectious disease is that the production of neutralising antibodies or recalled memory B and T cell responses potentially have a duration of at least 10 years, but different infections or diseases can have individually different immunological responses. Measles immunisation seemingly induces antibody types that completely block the method of viral entry to the cell and replication. The role of type I/III IFN in MeV infection remains unknown, and deficiencies can occur that affect both host viral and bacterial immune responses during development. At this time, 2 MeV accessory proteins (C/V) were examined that could interfere with the type I IFN receptor (IFNAR1) complex by binding to signal transducer and activator of transcription (STAT1) protein. Further details will be outlined in our next articles on the type I/II and type III IFN pathways during infectious diseases or immunodeficiency. Therefore, during natural MeV infection, innate immune responses may be independent of type I/III IFN synthesis, with much remaining unknown.

Currently, 129 clinical trials investigating measles infection have been completed, with 8 in progress (see Supplementary Materials). Beyond the outline above, comparatively much remains unknown on the mechanisms that MeV utilises within cells, but it is indicated to form inclusion bodies (IBs) within cells [14][75][76]. Given the above in research terms, clarity will further be required on other T cells affected by MeV infection. Despite the comparative success of immunisation to date and lack of antigenic variation, much remains unknown on a pathogen that has high transmission rates and predominantly affects infants under the age of 5. Future research should, therefore, consider the other T cell phenotypes and

transcriptome studies. Other recent studies before and since the recent SARS-CoV-2 pandemic are indicative that CD150 clearly has a role in DC maturation. Since other DC phenotypes were observed between 2006-2018 and specifically in 2017, further developments will be interesting to see [77][78].

Supplementary Materials: Manual for the Laboratory-based Surveillance of Measles, Rubella, and Congenital Rubella Syndrome - TechNet-21; Measles - Annual Epidemiological Report for 2022 (europa.eu): Measles - number of reported cases (who.int); WER9030_373-380.PDF (who.int); Search Results | Beta ClinicalTrials.gov; History of measles vaccination (who.int); human rabies immunoglobulin: List of nationally authorised medicinal products - PSUSA/00001639/201704 (europa.eu); Antibody therapeutics approved or in regulatory review in the EU or US - The Antibody Society; https://www.who.int/health-topics/poliomyelitis/

Declarations: None

Author contributions: BB: Conceptualisation, Methodology, Formal analysis, Writing—review & editing, Data curation, Writing—original draft, Visualization, Software, Supervision.

Conflicts of interest: The authors declare that they have no conflicts of interest.

Ethical approval: Not applicable.

Consent to participate: Not applicable.

Consent to publication: Informed consent to publication was obtained from relevant participants.

Availability of data and materials: Requests for accessing the datasets could be directed to the corresponding author (abrownbscmsc@gmail.com) or to Supplementary materials.

Funding: Not applicable.

References

1. [a, b, c] *Brown, B.; Gravier, T.; Fricke, I.; Al-Sheboul, S.A.; Carp, T.-N.; Leow, C.Y.; Imarogbe, C.; Arabpour, J. Immunopathogenesis of Nipah Virus Infection and Associated Immune Responses. Im-muno 2023, 3, 160-181, doi:10.3390/immuno3020011.*
2. [a, b, c, d] *Brown, B.; Ojha, V.; Fricke, I.; Al-Sheboul, S.A.; Imarogbe, C.; Gravier, T.; Green, M.; Peterson, L.; Koutsaroff, I.P.; Demir, A.; et al. Innate and Adaptive Immunity during SARS-CoV-2 Infection: Bi-omolecular Cellular Markers and Mechanisms. Vaccines (Basel) 2023, 11, 408, doi:10.3390/vaccines11020408.*
3. [a, b] *Brown, B. Dr Jekyll and Mr Hyde: From Two Branches of Immune Response to Three Types of In-terferon Response. 2023, doi:10.32388/PBXUF5.*
4. [^] *Lin, L.-T.; Richardson, C. The Host Cell Receptors for Measles Virus and Their Interaction with the Viral Hemagglutinin (H) Protein. Viruses 2016, 8, 250, doi:10.3390/v8090250.*

5. ^Ammour, Y.; Susova, O.; Krasnov, G.; Nikolaeva, E.; Varachev, V.; Schetinina, Y.; Gavrilova, M.; Mitrofanov, A.; Poletaeva, A.; Bekyashev, A.; et al. Transcriptome Analysis of Human Glioblastoma Cells Susceptible to Infection with the Leningrad-16 Vaccine Strain of Measles Virus. Viruses 2022, 14, 2433, doi:10.3390/v14112433.
6. ^Engeland, C.E.; Ungerechts, G. Measles Virus as an Oncolytic Immunotherapy. Cancers (Basel) 2021, 13, 544, doi:10.3390/cancers13030544.
7. ^Pidelaserra-Martí, G.; Engeland, C.E. Mechanisms of Measles Virus Oncolytic Immunotherapy. Cy-tokine Growth Factor Rev 2020, 56, 28-38, doi:10.1016/j.cytogfr.2020.07.009.
8. ^Frantz, P.N.; Teeravechyan, S.; Tangy, F. Measles-Derived Vaccines to Prevent Emerging Viral Dis-eases. Microbes Infect 2018, 20, 493-500, doi:10.1016/j.micinf.2018.01.005.
9. ^Gerke, C.; Frantz, P.N.; Ramsauer, K.; Tangy, F. Measles-Vectored Vaccine Approaches against Viral Infections: A Focus on Chikungunya. Expert Rev Vaccines 2019, 18, 393-403, doi:10.1080/14760584.2019.1562908.
10. ^Ebenig, A.; Lange, M. V.; Mühlebach, M.D. Versatility of Live-Attenuated Measles Viruses as Plat-form Technology for Recombinant Vaccines. NPJ Vaccines 2022, 7, 119, doi:10.1038/s41541-022-00543-4.
11. ^Guerra, F.M.; Bolotin, S.; Lim, G.; Heffernan, J.; Deeks, S.L.; Li, Y.; Crowcroft, N.S. The Basic Re-production Number (R 0) of Measles: A Systematic Review. Lancet Infect Dis 2017, 17, e420-e428, doi:10.1016/S1473-3099(17)30307-9.
12. ^Di Pietrantonj, C.; Rivetti, A.; Marchione, P.; Debalini, M.G.; Demicheli, V. Vaccines for Measles, Mumps, Rubella, and Varicella in Children. Cochrane Database of Systematic Reviews 2021, 2021, doi:10.1002/14651858.CD004407.pub5.
13. ^Baxter, D. Active and Passive Immunity, Vaccine Types, Excipients and Licensing. Occup Med (Chic Ill) 2007, 57, 552-556, doi:10.1093/occmed/kqm110.
14. a, b Guseva, S.; Milles, S.; Jensen, M.R.; Schoehn, G.; Ruigrok, R.W.; Blackledge, M. Structure, Dynam-ics and Phase Separation of Measles Virus RNA Replication Machinery. Curr Opin Virol 2020, 41, 59-67.
15. ^Zhou, Y.; Su, J.M.; Samuel, C.E.; Ma, D. Measles Virus Forms Inclusion Bodies with Properties of Liquid Organelles. J Virol 2019, 93, doi:10.1128/JVI.00948-19.
16. ^Kimura, H.; Saitoh, M.; Kobayashi, M.; Ishii, H.; Saraya, T.; Kurai, D.; Tsukagoshi, H.; Shirabe, K.; Nishina, A.; Kozawa, K.; et al. Molecular Evolution of Haemagglutinin (H) Gene in Measles Virus. Sci Rep 2015, 5, 11648, doi:10.1038/srep11648.
17. ^Schrag, S.J.; Rota, P.A.; Bellini, W.J. Spontaneous Mutation Rate of Measles Virus: Direct Estima-tion Based on Mutations Conferring Monoclonal Antibody Resistance. J Virol 1999, 73, 51-54, doi:10.1128/JVI.73.1.51-54.1999.
18. ^Gardy, J.L.; Naus, M.; Amlani, A.; Chung, W.; Kim, H.; Tan, M.; Severini, A.; Krajden, M.; Pud-dicombe, D.; Sahni, V.; et al. Whole-Genome Sequencing of Measles Virus Genotypes H1 and D8 During Outbreaks of Infection Following the 2010 Olympic Winter Games Reveals Viral Transmis-sion Routes. Journal of Infectious Diseases 2015, 212, 1574-1578, doi:10.1093/infdis/jiv271.
19. ^Brown, K.E.; Rota, P.A.; Goodson, J.L.; Williams, D.; Abernathy, E.; Takeda, M.; Mulders, M.N. Genetic Characterization of Measles and Rubella Viruses Detected Through Global Measles and Ru-bella Elimination Surveillance, 2016-2018. MMWR Morb Mortal Wkly Rep 2019, 68, 587-591, doi:10.15585/mmwr.mm6826a3.
20. ^Bianchi, S.; Canuti, M.; Ciceri, G.; Gori, M.; Colzani, D.; Dura, M.; Pennati, B.M.; Baggieri, M.; Magurano, F.; Tanzi,

E.; et al. Molecular Epidemiology of B3 and D8 Measles Viruses through He-magglutinin Phylogenetic History. Int J Mol Sci 2020, 21, 4435, doi:10.3390/ijms21124435.

21. [a, b]*Kemper, C.; Atkinson, J.P. Measles Virus and CD46. In Measles; Springer Berlin Heidelberg: Berlin, Heidelberg; pp. 31-57.*
22. [^]*Laksono, B.; de Vries, R.; McQuaid, S.; Duprex, W.; de Swart, R. Measles Virus Host Invasion and Pathogenesis. Viruses 2016, 8, 210, doi:10.3390/v8080210.*
23. [a, b]*Noyce, R.S.; Richardson, C.D. Nectin 4 Is the Epithelial Cell Receptor for Measles Virus. Trends Mi-crobiol 2012, 20, 429-439, doi:10.1016/j.tim.2012.05.006.*
24. [a, b]*Chatterjee, S.; Sinha, S.; Kundu, C.N. Nectin Cell Adhesion Molecule-4 (NECTIN-4): A Potential Target for Cancer Therapy. Eur J Pharmacol 2021, 911, 174516, doi:10.1016/j.ejphar.2021.174516.*
25. [^]*Liszewski, M.K.; Atkinson, J.P. Membrane Cofactor Protein (MCP; CD46): Deficiency States and Pathogen Connections. Curr Opin Immunol 2021, 72, 126-134, doi:10.1016/j.coi.2021.04.005.*
26. [^]*Noyce, R.S.; Richardson, C.D. Nectin 4 Is the Epithelial Cell Receptor for Measles Virus. Trends Mi-crobiol 2012, 20, 429-439, doi:10.1016/j.tim.2012.05.006.*
27. [a, b, c, d]*de Vries, R.D.; McQuaid, S.; van Amerongen, G.; Yüksel, S.; Verburgh, R.J.; Osterhaus, A.D.M.E.; Duprex, W.P.; de Swart, R.L. Measles Immune Suppression: Lessons from the Macaque Model. PLoS Pathog 2012, 8, e1002885, doi:10.1371/journal.ppat.1002885.*
28. [a, b]*Isa, M.B.; Martínez, L.; Giordano, M.; Zapata, M.; Passeggi, C.; De Wolff, M.C.; Nates, S. Measles Virus-Specific Immunoglobulin G Isotype Immune Response in Early and Late Infections. J Clin Mi-crobiol 2001, 39, 170-174, doi:10.1128/JCM.39.1.170-174.2001.*
29. [^]*Anichini, G.; Gandolfo, C.; Fabrizi, S.; Miceli, G.B.; Terrosi, C.; Gori Savellini, G.; Prathyumnan, S.; Orsi, D.; Battista, G.; Cusi, M.G. Seroprevalence to Measles Virus after Vaccination or Natural Infec-tion in an Adult Population, in Italy. Vaccines (Basel) 2020, 8, 66, doi:10.3390/vaccines8010066.*
30. [^]*Carryn, S.; Feyssaguet, M.; Povey, M.; Di Paolo, E. Long-Term Immunogenicity of Measles, Mumps and Rubella-Containing Vaccines in Healthy Young Children: A 10-Year Follow-Up. Vaccine 2019, 37, 5323-5331, doi:10.1016/j.vaccine.2019.07.049.*
31. [^]*Toptygina, A.P.; Pukhalsky, A.L.; Alioshkin, V.A. Immunoglobulin G Subclass Profile of Antimea-sles Response in Vaccinated Children and in Adults with Measles History. Clinical and Vaccine Im-munology 2005, 12, 845-847, doi:10.1128/CDLI.12.7.845-847.2005.*
32. [^]*Wang, F.; Tsai, J.C.; Davis, J.H.; Chau, B.; Dong, J.; West, S.M.; Hogan, J.M.; Wheeler, M.L.; Bee, C.; Morishige, W.; et al. Design and Characterization of Mouse IgG1 and IgG2a Bispecific Antibod-ies for Use in Syngeneic Models. MAbs 2020, 12, doi:10.1080/19420862.2019.1685350.*
33. [^]*Kao, D.; Danzer, H.; Collin, M.; Groß, A.; Eichler, J.; Stambuk, J.; Lauc, G.; Lux, A.; Nimmerjahn, F. A Monosaccharide Residue Is Sufficient to Maintain Mouse and Human IgG Subclass Activity and Directs IgG Effector Functions to Cellular Fc Receptors. Cell Rep 2015, 13, 2376-2385, doi:10.1016/j.celrep.2015.11.027.*
34. [^]*Vidarsson, G.; Dekkers, G.; Rispens, T. IgG Subclasses and Allotypes: From Structure to Effector Functions. Front Immunol 2014, 5, doi:10.3389/fimmu.2014.00520.*

35. [a, b]*Mina, M.J.; Kula, T.; Leng, Y.; Li, M.; de Vries, R.D.; Knip, M.; Siljander, H.; Rewers, M.; Choy, D.F.; Wilson, M.S.; et al. Measles Virus Infection Diminishes Preexisting Antibodies That Offer Pro-tection from Other Pathogens. Science (1979) 2019, 366, 599-606, doi:10.1126/science.aay6485.*
36. [^]*Mina, M.J.; Kula, T.; Leng, Y.; Li, M.; de Vries, R.D.; Knip, M.; Siljander, H.; Rewers, M.; Choy, D.F.; Wilson, M.S.; et al. Measles Virus Infection Diminishes Preexisting Antibodies That Offer Pro-tection from Other Pathogens. Science (1979) 2019, 366, 599-606, doi:10.1126/science.aay6485.*
37. [^]*de Vries, R.D.; McQuaid, S.; van Amerongen, G.; Yüksel, S.; Verburgh, R.J.; Osterhaus, A.D.M.E.; Duprex, W.P.; de Swart, R.L. Measles Immune Suppression: Lessons from the Macaque Model. PLoS Pathog 2012, 8, e1002885, doi:10.1371/journal.ppat.1002885.*
38. [^]*de Vries, R.; Duprex, W.; de Swart, R. Morbillivirus Infections: An Introduction. Viruses 2015, 7, 699-706, doi:10.3390/v7020699.*
39. [a, b]*Brown, B. Innate and Adaptive Immune Response during Ebola and Filoviridae Infection: A Cellular Analysis to 2023., doi:10.13140/RG.2.2.24216.57603.*
40. [^]*Lutz, C.S.; Hasan, A.Z.; Bolotin, S.; Crowcroft, N.S.; Cutts, F.T.; Joh, E.; Loisate, S.; Moss, W.J.; Osman, S.; Hayford, K. Comparison of Measles IgG Enzyme Immunoassays (EIA) versus Plaque Re-duction Neutralization Test (PRNT) for Measuring measles serostatus: A Systematic Review of Head-to-Head Analyses of Measles IgG EIA and PRNT. BMC Infect Dis 2023, 23, 367, doi:10.1186/s12879-023-08199-8.*
41. [a, b]*Laksono, B.M.; de Vries, R.D.; Verburgh, R.J.; Visser, E.G.; de Jong, A.; Fraaij, P.L.A.; Ruijs, W.L.M.; Nieuwenhuijse, D.F.; van den Ham, H.-J.; Koopmans, M.P.G.; et al. Studies into the Mecha-nism of Measles-Associated Immune Suppression during a Measles Outbreak in the Netherlands. Nat Commun 2018, 9, 4944, doi:10.1038/s41467-018-07515-0.*
42. [^]*Petrova, V.N.; Sawatsky, B.; Han, A.X.; Laksono, B.M.; Walz, L.; Parker, E.; Pieper, K.; Anderson, C.A.; de Vries, R.D.; Lanzavecchia, A.; et al. Incomplete Genetic Reconstitution of B Cell Pools Con-tributes to Prolonged Immunosuppression after Measles. Sci Immunol 2019, 4, doi:10.1126/sciimmunol.aay6125.*
43. [^]*Sánchez-Martín, L.; Estecha, A.; Samaniego, R.; Sánchez-Ramón, S.; Vega, M.Á.; Sánchez-Mateos, P. The Chemokine CXCL12 Regulates Monocyte-Macrophage Differentiation and RUNX3 Expres-sion. Blood 2011, 117, 88-97, doi:10.1182/blood-2009-12-258186.*
44. [^]*Cambier, S.; Gouwy, M.; Proost, P. The Chemokines CXCL8 and CXCL12: Molecular and Function-al Properties, Role in Disease and Efforts towards Pharmacological Intervention. Cell Mol Immunol 2023, 20, 217-251, doi:10.1038/s41423-023-00974-6.*
45. [^]*Haralambieva, I.H.; Zimmermann, M.T.; Ovsyannikova, I.G.; Grill, D.E.; Oberg, A.L.; Kennedy, R.B.; Poland, G.A. Whole Transcriptome Profiling Identifies CD93 and Other Plasma Cell Survival Factor Genes Associated with Measles-Specific Antibody Response after Vaccination. PLoS One 2016, 11, e0160970, doi:10.1371/journal.pone.0160970.*
46. [a, b]*Zhang, Z.; Zheng, M.; Ding, Q.; Liu, M. CD93 Correlates With Immune Infiltration and Impacts Pa-tient Immunotherapy Efficacy: A Pan-Cancer Analysis. Front Cell Dev Biol 2022, 10, doi:10.3389/fcell.2022.817965.*
47. [^]*Nativel, B.; Ramin-Mangata, S.; Mevizou, R.; Figuester, A.; Andries, J.; Iwema, T.; Ikewaki, N.; Gasque, P.; Viranaïcken, W. CD93 Is a Cell Surface Lectin Receptor Involved in the Control of the Inflammatory Response*

Stimulated by Exogenous DNA. Immunology 2019, 158, 85-93, doi:10.1111/imm.13100.

48. ^*Haralambieva, I.H.; Zimmermann, M.T.; Ovsyannikova, I.G.; Grill, D.E.; Oberg, A.L.; Kennedy, R.B.; Poland, G.A. Whole Transcriptome Profiling Identifies CD93 and Other Plasma Cell Survival Factor Genes Associated with Measles-Specific Antibody Response after Vaccination. PLoS One 2016, 11, e0160970, doi:10.1371/journal.pone.0160970.*
49. a, b*Nelson, A.N.; Putnam, N.; Hauer, D.; Baxter, V.K.; Adams, R.J.; Griffin, D.E. Evolution of T Cell Responses during Measles Virus Infection and RNA Clearance. Sci Rep 2017, 7, 11474, doi:10.1038/s41598-017-10965-z.*
50. ^*Eberl, G. RORγt, a Multitask Nuclear Receptor at Mucosal Surfaces. Mucosal Immunol 2017, 10, 27-34, doi:10.1038/mi.2016.86.*
51. ^*Semmler, G.; Griebler, H.; Aberle, S.W.; Stiasny, K.; Richter, L.; Holzmann, H.; Weseslindtner, L. Elevated CXCL10 Serum Levels in Measles Virus Primary Infection and Reinfection Correlate With the Serological Stage and Hospitalization Status. J Infect Dis 2020, 222, 2030-2034, doi:10.1093/infdis/jiaa326.*
52. ^*Allen, I. V.; McQuaid, S.; Penalva, R.; Ludlow, M.; Duprex, W.P.; Rima, B.K. Macrophages and Dendritic Cells Are the Predominant Cells Infected in Measles in Humans. mSphere 2018, 3, doi:10.1128/mSphere.00570-17.*
53. ^*Sato, H.; Hoshi, M.; Ikeda, F.; Fujiyuki, T.; Yoneda, M.; Kai, C. Downregulation of Mitochondrial Biogenesis by Virus Infection Triggers Antiviral Responses by Cyclic GMP-AMP Synthase. PLoS Pathog 2021, 17, e1009841, doi:10.1371/journal.ppat.1009841.*
54. a, b*Brown, B.; Gravier, T.; Carpe, T.; Fricke, I. Dr Jekyll and Mr Hyde: From Two Branches of Immune Response to Three Types of Interferon Response SARS-CoV-2 and PRR View Project Localization of Cold Shock Proteins View Project Dr Jekyll and Mr Hyde: From Two Branches of Immune Re-Sponse to Three Types of Interferon Response., doi:10.13140/RG.2.2.18873.75368.*
55. ^*Rudak, P.T.; Yao, T.; Richardson, C.D.; Haeryfar, S.M.M. Measles Virus Infects and Programs MAIT Cells for Apoptosis. J Infect Dis 2021, 223, 667-672, doi:10.1093/infdis/jiaa407.*
56. ^*Flores-Villanueva, P.; Sobhani, N.; Wang, X.; Li, Y. MR1-Restricted T Cells in Cancer Immunother-apy. Cancers (Basel) 2020, 12, 2145, doi:10.3390/cancers12082145.*
57. ^*Chancellor, A.; Vacchini, A.; De Libero, G. MR1, an Immunological Periscope of Cellular Metabo-lism. Int Immunol 2022, 34, 141-147, doi:10.1093/intimm/dxab101.*
58. ^*Rodan Sarohan, A. STRA6: The Key to Inflammatory Pathways in COVID-19. Fortune Journal of Health Sciences 2023, 06, doi:10.26502/fjhs.098.*
59. ^*Dhokia, V.; Macip, S. A Master of All Trades - Linking Retinoids to Different Signalling Pathways through the Multi-Purpose Receptor STRA6. Cell Death Discov 2021, 7, 358, doi:10.1038/s41420-021-00754-z.*
60. ^*Blaner, W.S. STRA6, a Cell-Surface Receptor for Retinol-Binding Protein: The Plot Thickens. Cell Metab 2007, 5, 164-166, doi:10.1016/j.cmet.2007.02.006.*
61. ^*Perriman, L.; Tavakolinia, N.; Jalali, S.; Li, S.; Hickey, P.F.; Amann-Zalcenstein, D.; Ho, W.W.H.; Baldwin, T.M.; Piers, A.T.; Konstantinov, I.E.; et al. A Three-Stage Developmental Pathway for Hu-man Vγ9Vδ2 T Cells within the Postnatal Thymus. Sci Immunol 2023, 8, doi:10.1126/sciimmunol.abo4365.*
62. ^*Griffin, D.E. Measles Vaccine. Viral Immunol 2018, 31, 86-95, doi:10.1089/vim.2017.0143.*
63. ^*Jang, B.; Kim, H.W.; Kim, H.-S.; Park, J.Y.; Seo, H.; Kim, Y.K. Measles Virus Neutralizing Anti-body Response and*

Durability Two Years after One or Two Doses of Measles-Mumps-Rubella Vac-cine among Young Seronegative Healthcare Workers. Vaccines (Basel) 2022, 10, 1812, doi:10.3390/vaccines10111812.

64. ^*Bianchi, F.P.; Mascipinto, S.; Stefanizzi, P.; De Nitto, S.; Germinario, C.; Tafuri, S. Long-Term Im-munogenicity after Measles Vaccine vs. Wild Infection: An Italian Retrospective Cohort Study. Hum Vaccin Immunother 2021, 17, 2078-2084, doi:10.1080/21645515.2020.1871296.*
65. ^*Wang, Q.; Wang, W.; Winter, A.K.; Zhan, Z.; Ajelli, M.; Trentini, F.; Wang, L.; Li, F.; Yang, J.; Xiang, X.; et al. Long-Term Measles Antibody Profiles Following Different Vaccine Schedules in China, a Longitudinal Study. Nat Commun 2023, 14, 1746, doi:10.1038/s41467-023-37407-x.*
66. ^*Hassouneh, F.; Goldeck, D.; Pera, A.; van Heemst, D.; Slagboom, P.E.; Pawelec, G.; Solana, R. Func-tional Changes of T-Cell Subsets with Age and CMV Infection. Int J Mol Sci 2021, 22, 9973, doi:10.3390/ijms22189973.*
67. ^*Al-Sheboul, S.A.; Brown, B.; Shboul, Y.; Fricke, I.; Imarogbe, C.; Alzoubi, K.H. An Immunological Review of SARS-CoV-2 Infection and Vaccine Serology: Innate and Adaptive Responses to MRNA, Adenovirus, Inactivated and Protein Subunit Vaccines. Vaccines (Basel) 2022, 11, 51, doi:10.3390/vaccines11010051.*
68. ^*Yokota, S.; Saito, H.; Kubota, T.; Yokosawa, N.; Amano, K.; Fujii, N. Measles Virus Suppresses In-terferon-α Signaling Pathway: Suppression of Jak1 Phosphorylation and Association of Viral Acces-sory Proteins, C and V, with Interferon-α Receptor Complex. Virology 2003, 306, 135-146, doi:10.1016/S0042-6822(02)00026-0.*
69. ^*Shivakoti, R.; Hauer, D.; Adams, R.J.; Lin, W.-H.W.; Duprex, W.P.; de Swart, R.L.; Griffin, D.E. Limited In Vivo Production of Type I or Type III Interferon After Infection of Macaques with Vac-cine or Wild-Type Strains of Measles Virus. Journal of Interferon & Cytokine Research 2015, 35, 292-301, doi:10.1089/jir.2014.0122.*
70. ^*Shaffer, J.A.; Bellini, W.J.; Rota, P.A. The C Protein of Measles Virus Inhibits the Type I Interferon Response. Virology 2003, 315, 389-397, doi:10.1016/S0042-6822(03)00537-3.*
71. ^*Torracinta, L.; Tanner, R.; Vanderslott, S. MMR Vaccine Attitude and Uptake Research in the United Kingdom: A Critical Review. Vaccines (Basel) 2021, 9, 402, doi:10.3390/vaccines9040402.*
72. ^*Esolen, L.M.; Ward, B.J.; Moench, T.R.; Griffin, D.E. Infection of Monocytes during Measles. J In-fect Dis 1993, 168, 47-52, doi:10.1093/infdis/168.1.47.*
73. ^*Sullivan, J.L.; Barry, D.W.; Lucas, S.J.; Albrecht, P. Measles Infection of Human Mononuclear Cells. I. Acute Infection of Peripheral Blood Lymphocytes and Monocytes. Journal of Experimental Medi-cine 1975, 142, 773-784, doi:10.1084/jem.142.3.773.*
74. ^*GRIFFIN, D.E.; WARD, B.J.; JAUREGUI, E.; JOHNSON, R.T.; VAISBERG, A. Natural Killer Cell Activity during Measles. Clin Exp Immunol 2008, 81, 218-224, doi:10.1111/j.1365-2249.1990.tb03321.x.*
75. ^*Gadroen, K.; Dodd, C.N.; Masclee, G.M.C.; de Ridder, M.A.J.; Weibel, D.; Mina, M.J.; Grenfell, B.T.; Sturkenboom, M.C.J.M.; van de Vijver, D.A.M.C.; de Swart, R.L. Impact and Longevity of Measles-Associated Immune Suppression: A Matched Cohort Study Using Data from the THIN Gen-eral Practice Database in the UK. BMJ Open 2018, 8, e021465, doi:10.1136/bmjopen-2017-021465.*
76. ^*Arbore, G.; West, E.E.; Rahman, J.; Le Friec, G.; Niyonzima, N.; Pirooznia, M.; Tunc, I.; Pavlidis, P.; Powell, N.; Li, Y.; et al. Complement Receptor CD46 Co-Stimulates Optimal Human CD8+ T Cell Effector Function via Fatty Acid Metabolism. Nat Commun 2018, 9, 4186, doi:10.1038/s41467-018-06706-z.*

77. ^de Witte, L.; Abt, M.; Schneider-Schaulies, S.; van Kooyk, Y.; Geijtenbeek, T.B.H. Measles Virus Targets DC-SIGN To Enhance Dendritic Cell Infection. J Virol 2006, 80, 3477-3486, doi:10.1128/JVI.80.7.3477-3486.2006.

78. ^Derakhshani, S.; Kurz, A.; Japtok, L.; Schumacher, F.; Pilgram, L.; Steinke, M.; Kleuser, B.; Sauer, M.; Schneider-Schaulies, S.; Avota, E. Measles Virus Infection Fosters Dendritic Cell Motility in a 3D Environment to Enhance Transmission to Target Cells in the Respiratory Epithelium. Front Im-munol 2019, 10, doi:10.3389/fimmu.2019.01294.