

**Globoside Receptor of Human Parvovirus B19 is Dispensable for Virus Binding, Uptake and Nuclear Targeting but is Required for the Infection**

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Human parvovirus B19 (B19V) has a highly restricted cell tropism infecting exclusively erythroid progenitor cells at the differentiation stage from CFU-E to early erythroblasts. B19V utilizes globoside (Gb4Cer) as primary receptor. However, the restricted tropism is determined by as-yet-unknown co-receptor, which interacts with the N-terminal region of the VP1, and it is required for virus uptake into permissive cells. With the aim to elucidate the role of Gb4Cer in B19V infection, we have knocked out the gene B3GalNT1 from UT7-Epo cells, which encodes for the enzyme globoside synthase required for the biosynthesis of Gb4Cer. As a result, B3GalNT1 mRNA and Gb4Cer became undetectable in the knockout cells without affecting cell viability and proliferation. B19V was able to bind and internalize Gb4Cer KO cells, however, the infection was prevented. Engineered bacteriophage MS2 capsids with chemically coupled N-VP1 of B19V were able to bind and internalize wild-type and Gb4Cer KO cells. Isolation of purified nuclei from infected KO cells demonstrated that incoming B19V particles were able to reach the nuclei. These results together demonstrate that Gb4Cer is dispensable for virus binding, uptake, intracellular trafficking and import of incoming capsids into the nucleus, however, the presence of the receptor is still required to initiate the infection.