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Early phase clinical drug development for HPV-induced disorders: novel tools and treatments

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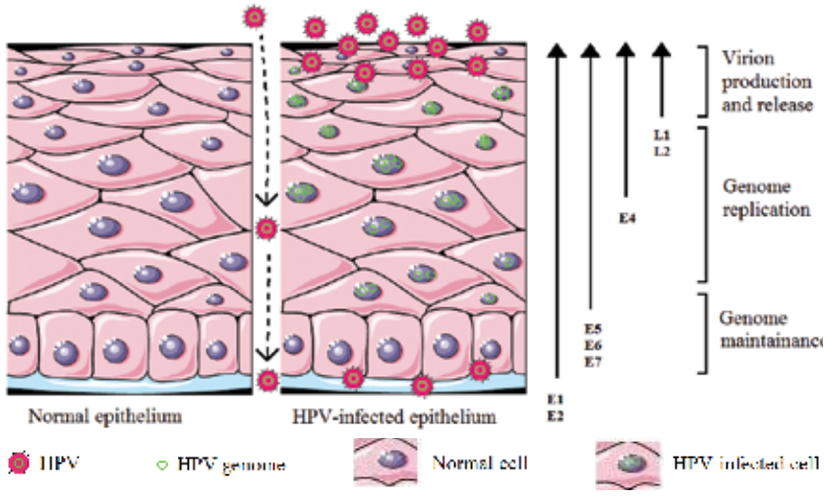
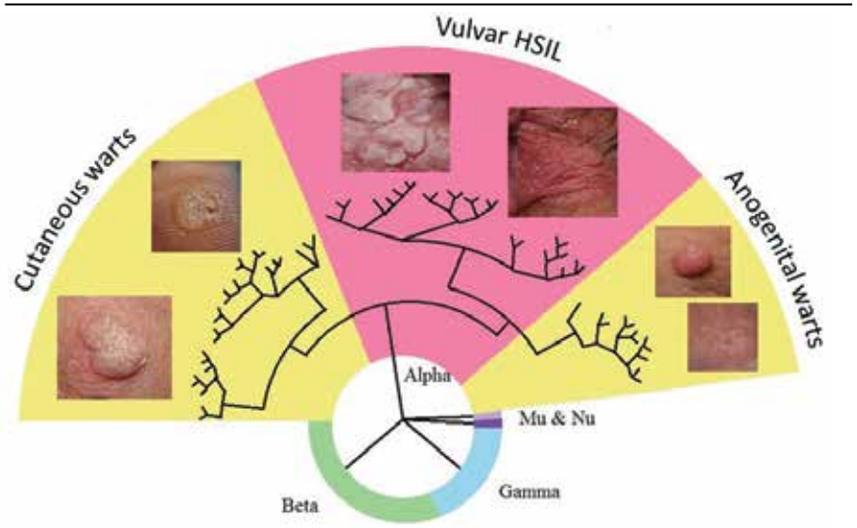
Chapter 1 – Figure 1. Genome organization of the Alpha papillomavirus HPV16. The genome is comprised of a long control region (LCR) and eight genes that are involved in the virus life cycle. This figure is adapted from de Sanjosé 2018 and Doorbar 2015.[9,10]

E1+E2:	Genome replication	E6+E7:	Oncogenes
E4:	Virus release and transmission	L1:	Major capsid protein
E5:	Evading immune response and apoptosis	L2:	Minor capsid protein
		LCR:	Long control region

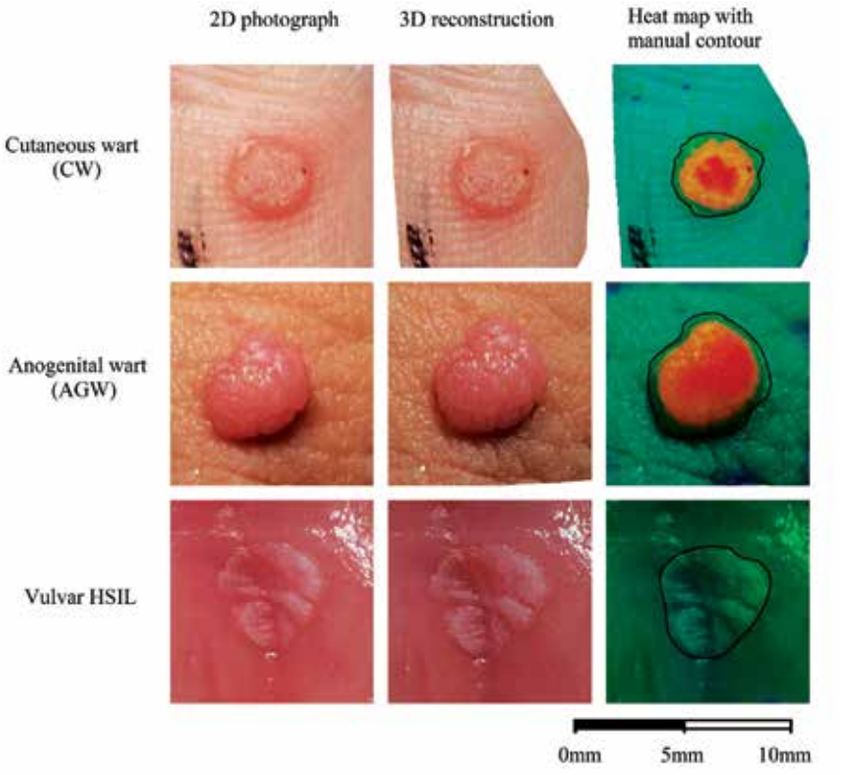
Chapter 1 – Figure 2. The life cycle of a HPV infection. A diagrammatic representation of the skin is shown after infection with HPV. Often a micro-trauma of the epithelium allows the virus to infect cells in the basal layer of the epithelium (dotted arrow lines). In the basal epithelial cells the virions are internalized and the viral genomes are transferred to the nucleus (genome maintenance). The genome of the virus is replicated in the nucleus and hereafter the virus particles are produced and released. The involvement of the early and late genes is shown with the arrows next to the figure. This figure is adapted from Doorbar 2005.[4]



Chapter 1 – Figure 3. Phylogenetic tree of human papilloma virus (HPV) demonstrating their evolutionary relationship. HPV types are divided in 5 different groups: Alpha (pink and yellow), Beta (green), Gamma (blue), Mu (purple) and Nu (lilac). The Alpha-papillomaviruses are subdivided as low-risk (yellow) and high-risk (pink) based on the benign or malignant potential of the virus, respectively. Cutaneous warts are caused by low-risk HPV types of the Alpha genus. Typical appearances of a common wart on the hand (left) and a plantar wart (right) are shown. Anogenital warts are also caused by low-risk HPV types of the Alpha genus, but these are phylogenetically different from the HPV types causing cutaneous warts as shown in the tree by the division of the branches. Anogenital warts on the penile shaft (upper) and under the foreskin (lower) are shown. High-risk HPV types of the Alpha genus (pink) cause vulvar high-grade squamous intraepithelial lesions (HSIL) with a high degree of variation in appearance, such as elevated hyperkeratotic white lesions (left) or red lesions (right).



Chapter 3 – Figure 1. 3D reconstruction of the twelve inch ruler (A) and wart-like object (B). Three-D reconstruction of the twelve inch ruler by the image reconstruction software (A), and the wart-like object in a 3D reconstruction with a heat-map showing the height of the object which is used for the 3D analysis (B).



SEE INSIDE FOR COLOR ILLUSTRATIONS OF CHAPTER 1 AND 3

EARLY PHASE CLINICAL DRUG DEVELOPMENT FOR HPV-INDUCED DISORDERS:
NOVEL TOOLS AND TREATMENTS

EARLY PHASE CLINICAL DRUG DEVELOPMENT FOR HPV-INDUCED DISORDERS: NOVEL TOOLS AND TREATMENTS

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