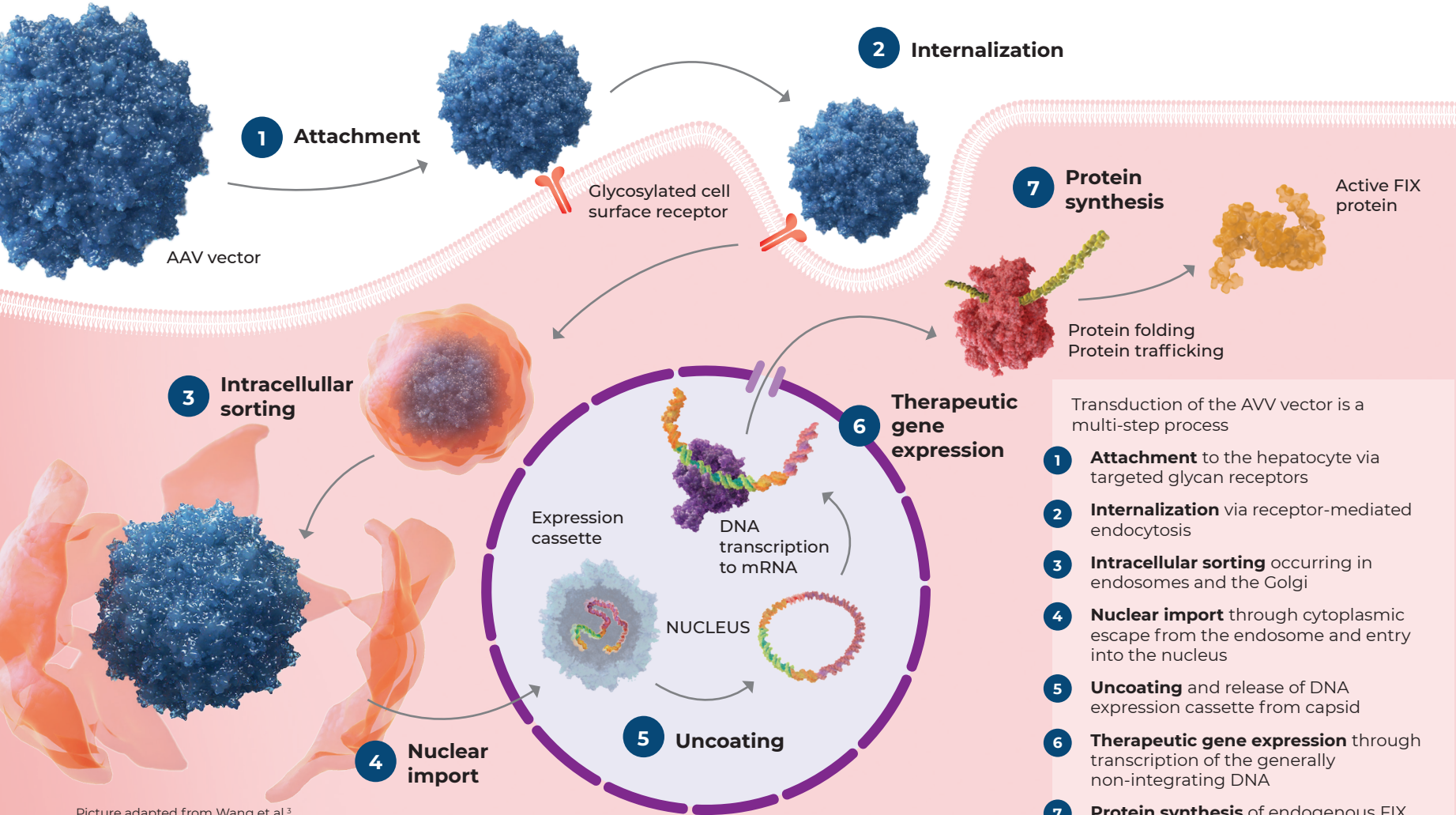
Gene therapy for treating disease

The gene therapies being studied in hemophilia B use recombinant AAV vectors for *in vivo*, liver-directed gene transfer with the goal of achieving durable, endogenous expression of functional FIX to restore hemostasis[1,2]



Transduction of the AVV vector is a multi-step process

1. **Attachment** to the hepatocyte via targeted glycan receptors
2. **Internalization** via receptor-mediated endocytosis
3. **Intracellular sorting** occurring in endosomes and the Golgi
4. **Nuclear import** through cytoplasmic escape from the endosome and entry into the nucleus
5. **Uncoating** and release of DNA expression cassette from capsid
6. **Therapeutic gene expression** through transcription of the generally non-integrating DNA
7. **Protein synthesis** of endogenous FIX to export to the bloodstream

Picture adapted from Wang et al.[3]
AAV=adeno-associated virus, FIX=factor IX.

1. Pipe S, et al. *Mol Ther Methods Clin Dev.* 2019;15:170-178. **2.** Srivastava A, et al. *Haemophlia.* 2020;26(suppl 6):1-158. **3.** Wang D, et al. *Nat Rev Drug Discov.* 2019;18(5):358-378.