

Department of Medicine, Division of Infectious Diseases &
Corporal Michael J. Crescenz VA Medical Center (Philadelphia VA)

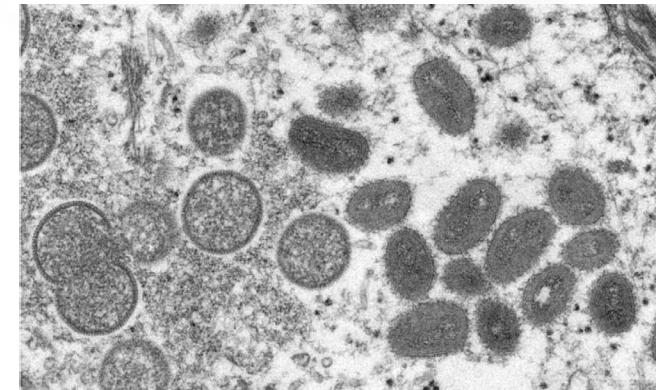
Orthopoxvirus pathogenesis and where we stand with therapeutics

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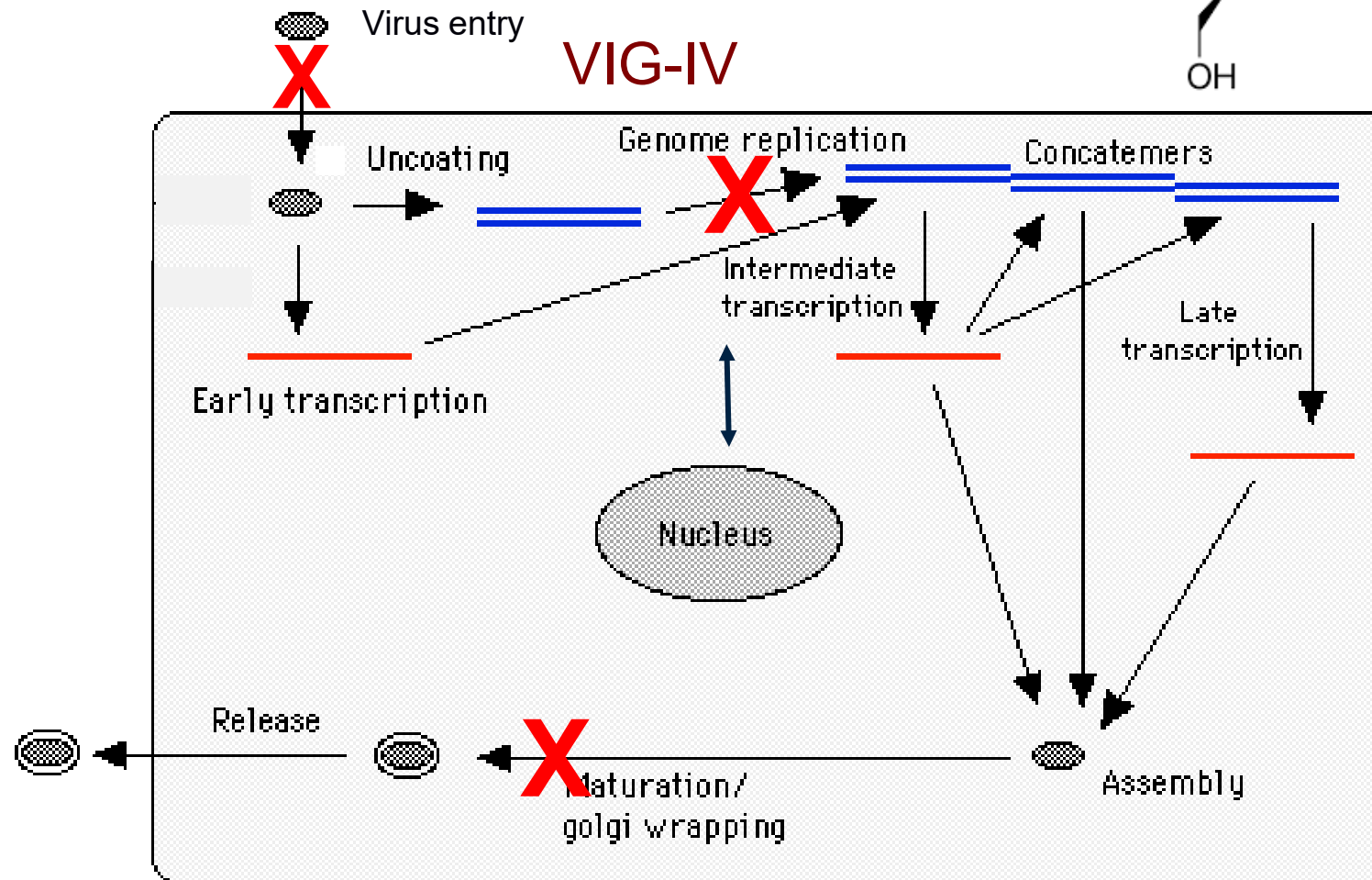
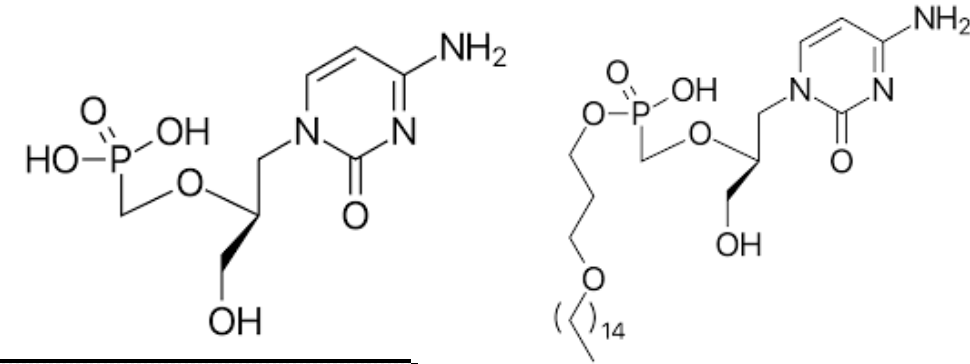
National Academies of Sciences, Engineering, and Medicine

Committee on the Current State of Research, Development, and Stockpiling of Smallpox Medical Countermeasures

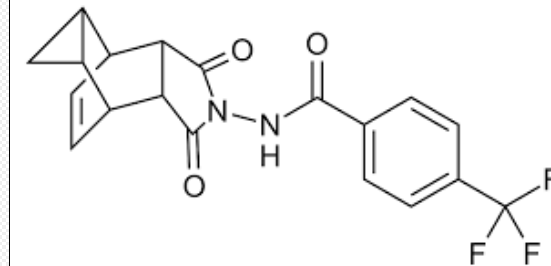


Poxvirus life cycle

(available therapeutics)

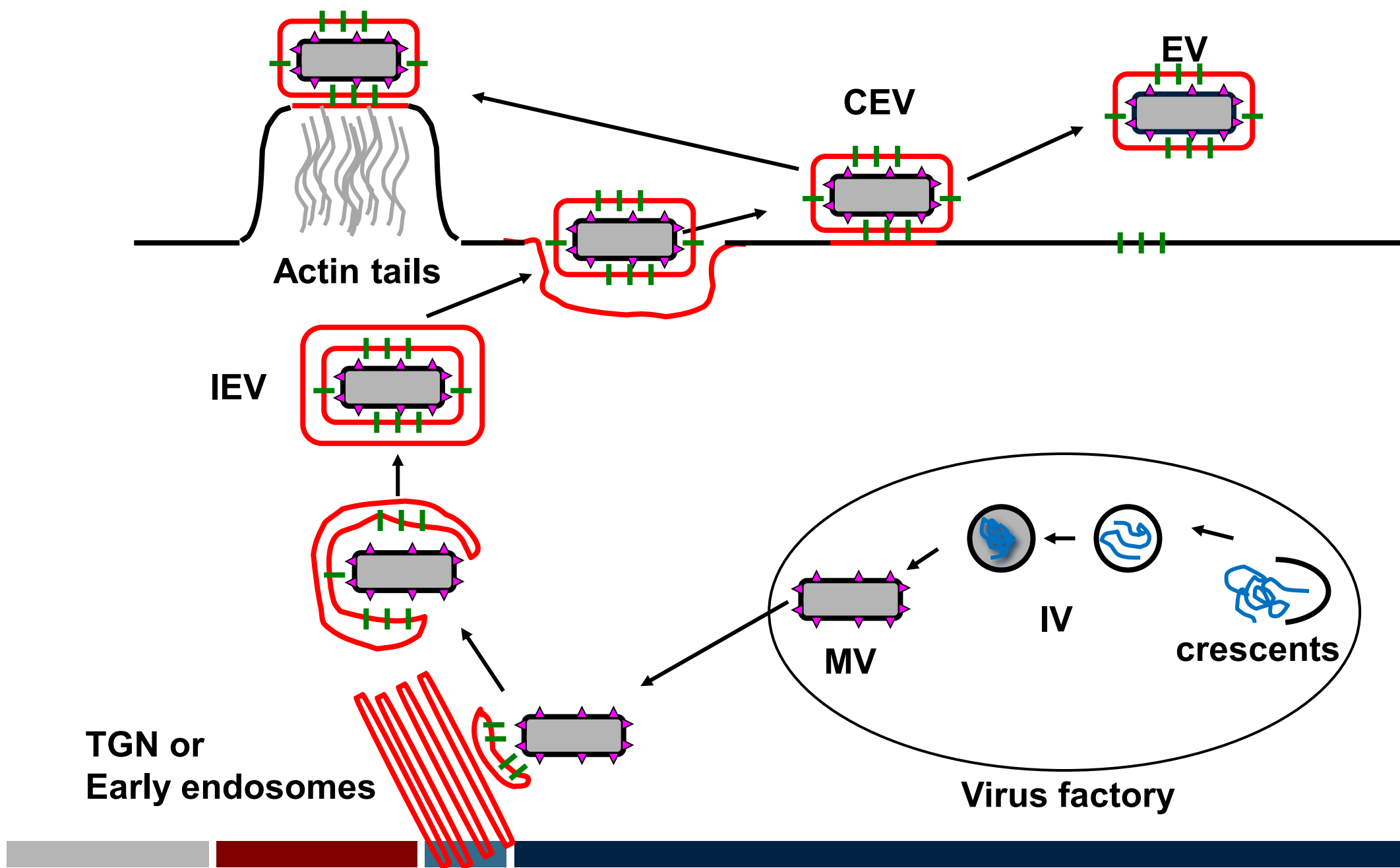


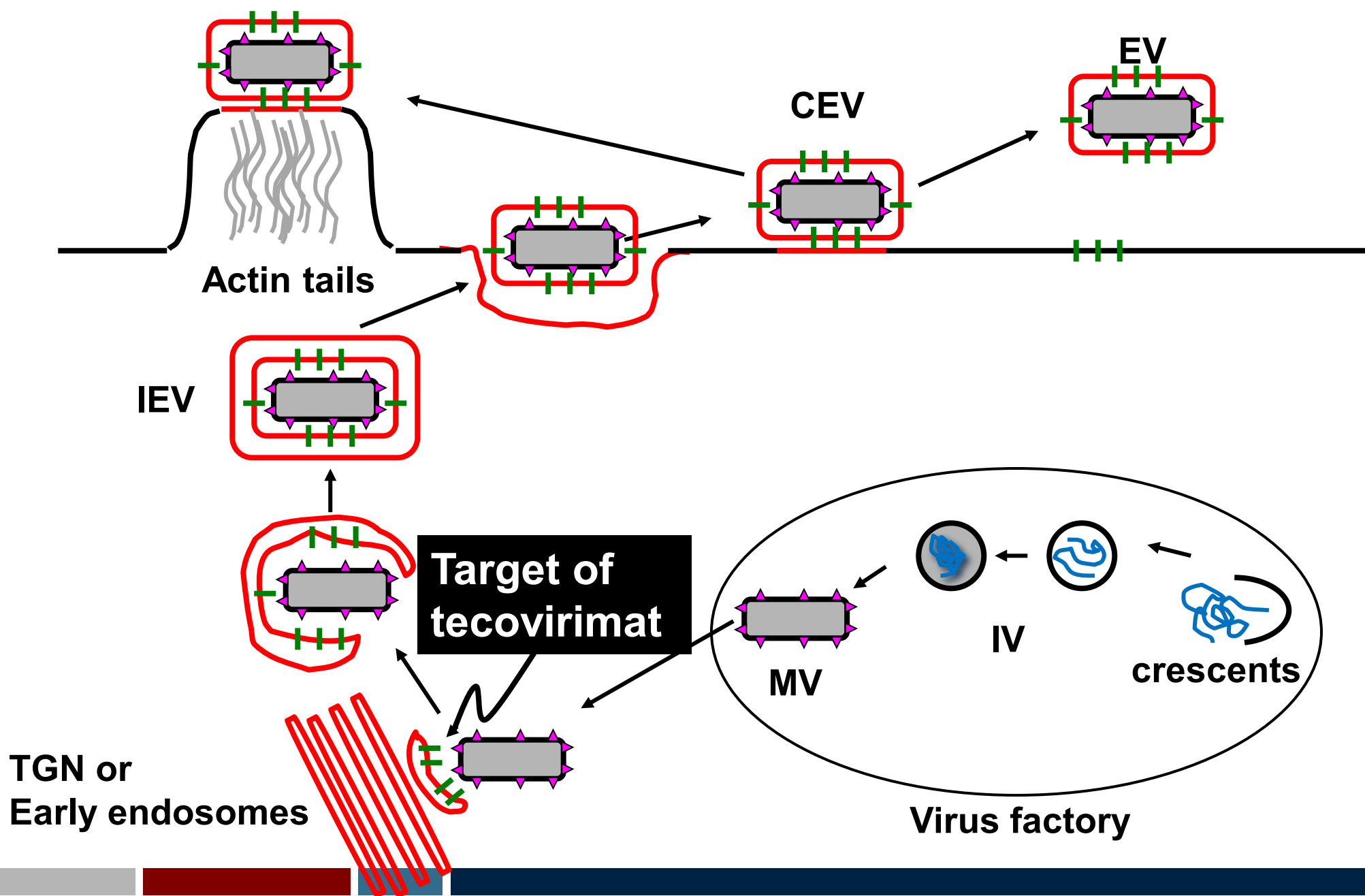
cidofovir (iv)
brincidofovir (po)



tecovirimat
(po or iv)







NHP challenge with monkeypox virus

	Tecovirimat (10 mg/kg) q24-h x 14 days		Brincidofovir	
Day treatment started post-infection	5x10 ⁷ pfu (i.v.)			
	Placebo	Tecovirimat		
4 (study 1)	0% (0/7)	80% (4/5)		
4 (study 2)	0% (0/6)	100% (6/6)		
4 (study 3)	0% (0/3)	83% (5/6)		
5		83% (5/6)		
6		50% (3/6)		

Mouse challenge with ectromelia virus

	Tecovirimat		Brincidofovir (10/5/5 mg/kg) q48-h x 3 doses	
Day treatment started post-infection			200 pfu (i.d.)	
			Placebo	Brincidofovir
4				66% (25/32)
5			13% (4/32)	66% (21/32)
6				34% (11/32)

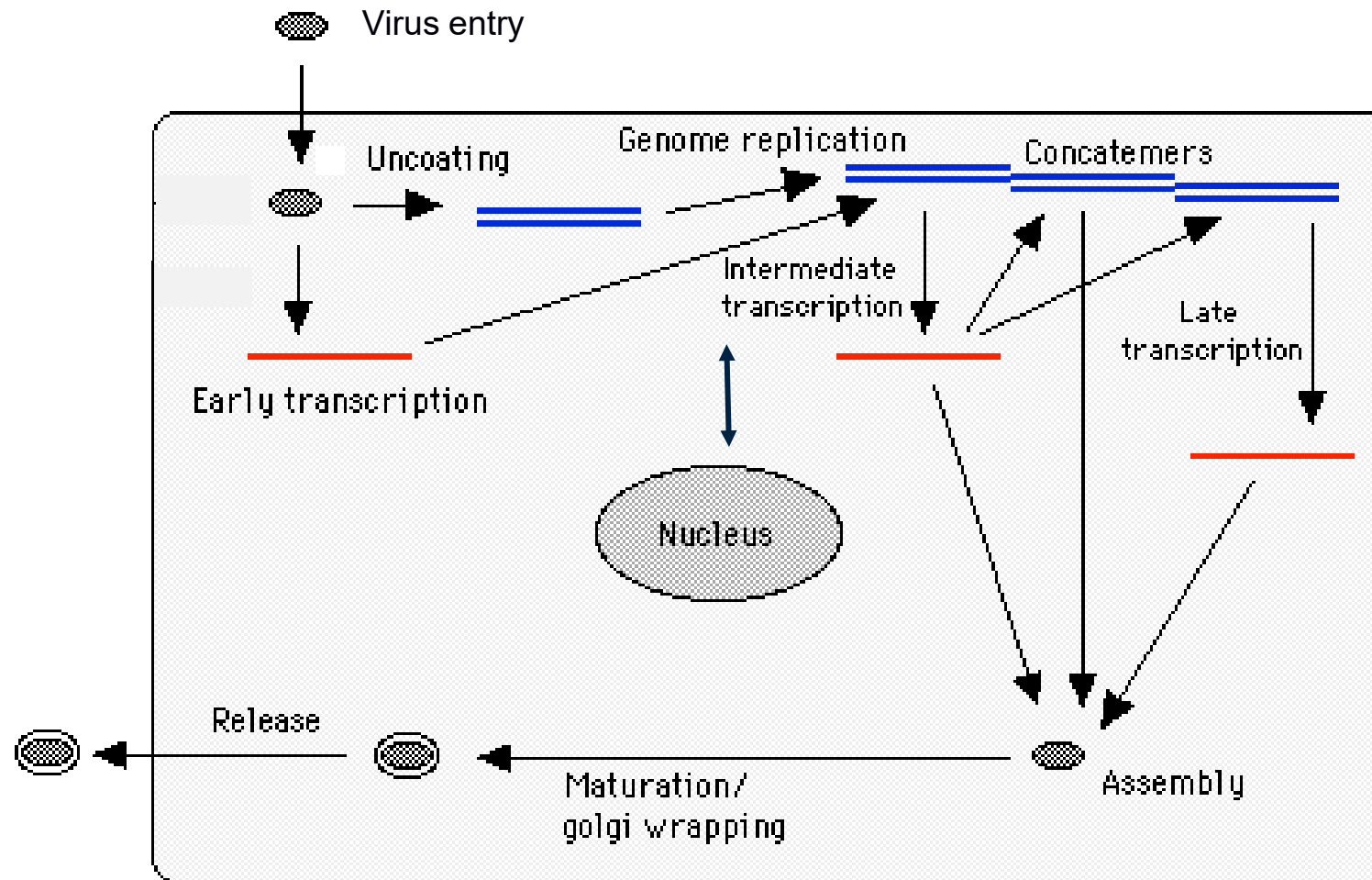
Rabbit challenge with rabbitpox virus

	Tecovirimat (40 mg/kg) q24-h x 14 days		Brincidofovir (20/5/5 mg/kg) q48-h x 3 doses	
Day treatment started post-infection	1,000 pfu (i.d.)		600 pfu (i.d.)	
	Placebo	Tecovirimat	Placebo	Brincidofovir
4	0% (0/10)	90% (9/10)*	29% (8/28)	90% (26/29)
5				69% (20/29)
6				69% (20/29)

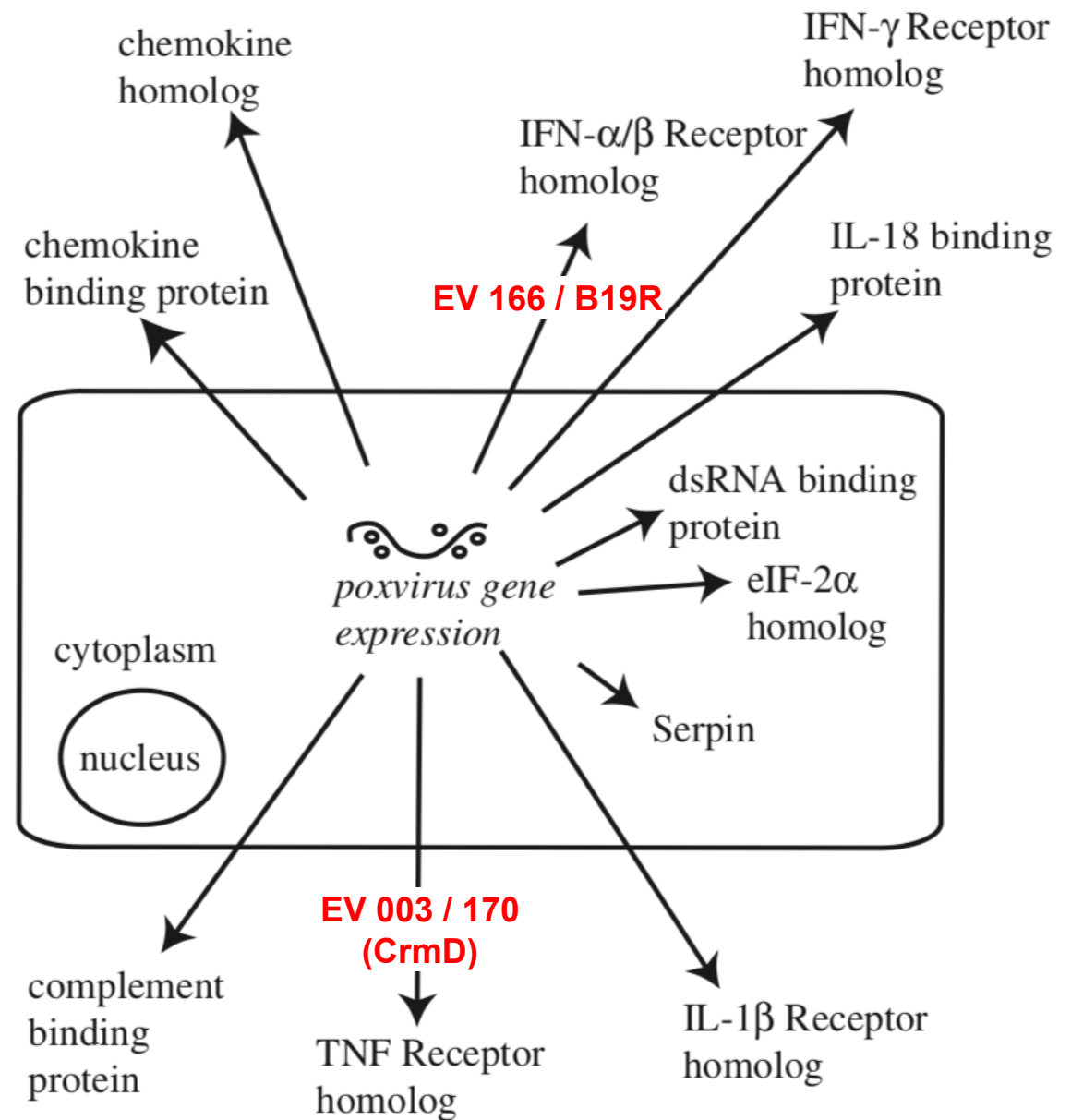
* Repeat 88% (7/8)

Poxvirus life cycle

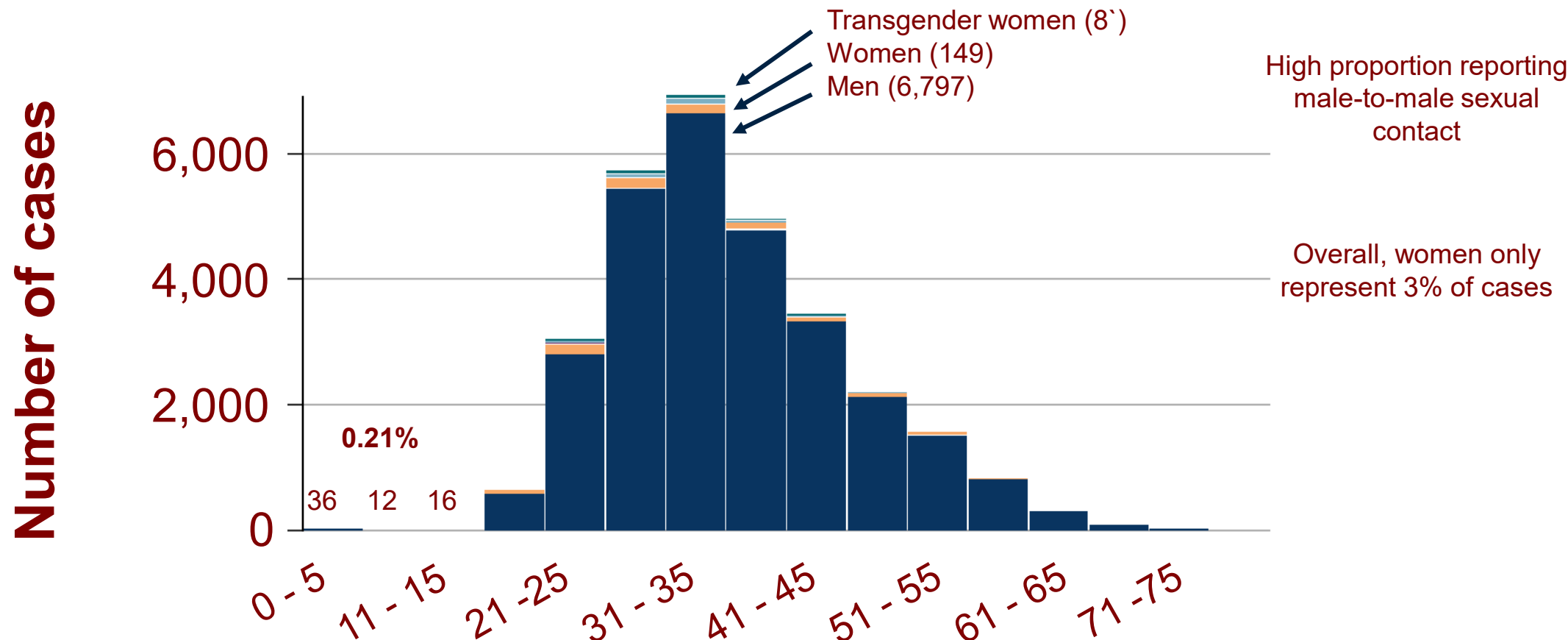
(Other therapeutic targets)



Poxvirus immune evasion proteins as therapeutic targets (simplified diagram)



U.S. Monkeypox cases reported to CDC: Age and Gender (30,969 cases)



9/28/23

ORTHOPOXVIRUS PATHOGENESIS AND WHERE WE STAND WITH THERAPEUTICS

NATIONAL ACADEMIES OF SCIENCES, ENGINEERING, AND MEDICINE

COMMITTEE ON THE CURRENT STATE OF RESEARCH, DEVELOPMENT, AND STOCKPILING OF
SMALLPOX MEDICAL COUNTERMEASURES



Penn Medicine

Questions and Discussion

