- Somatic
- Germinal

Animal Models 1.0, Natural
Animal Models 2.0, Transgenics
Animal Models 3.0, Cyborgs

The last 15 years of Neuroscience research have Led to an explosion in the use of physical engineering and synthetic biology in animals.

Artificial Proteins

Opsins
CRISPR
DREADDs

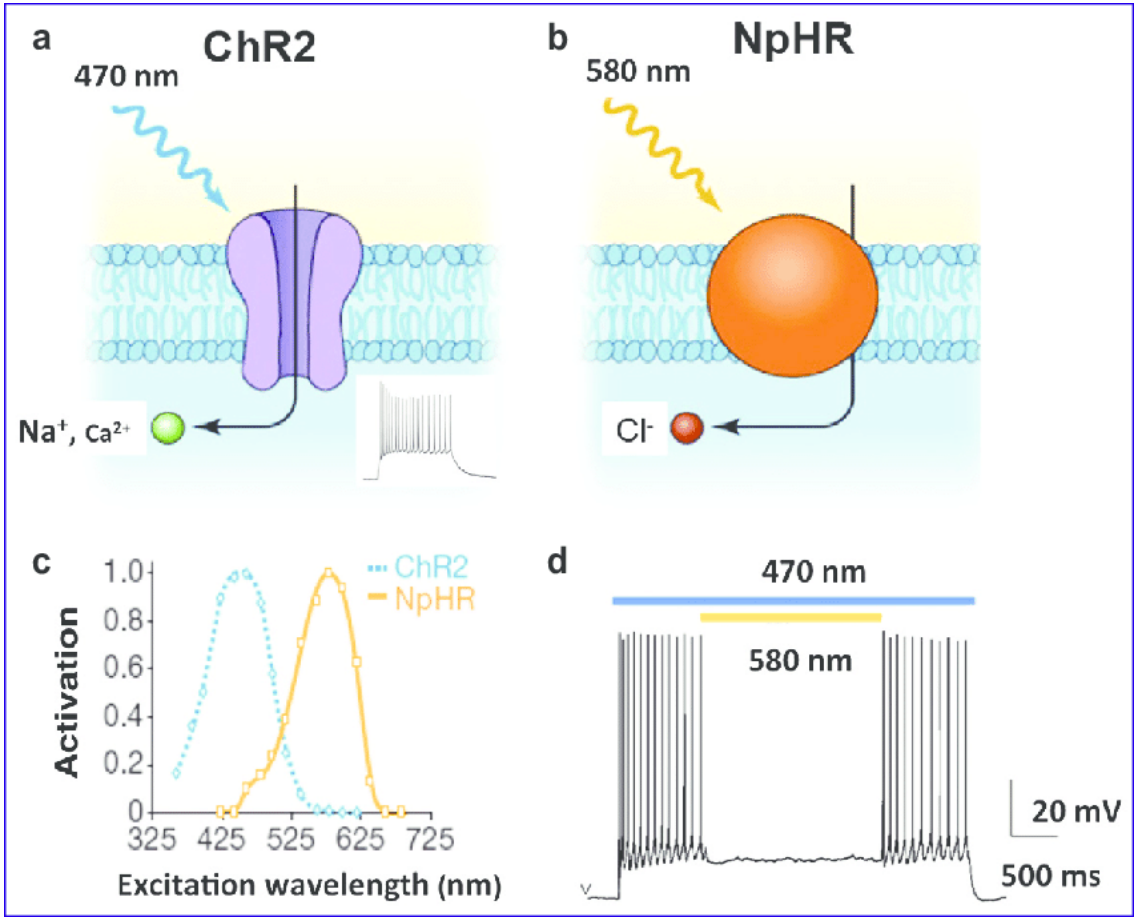
Optogenetic
Chemogenetic
Intersectional Genetic

Animal models have become very controlled system

The Tools #1. Opsins

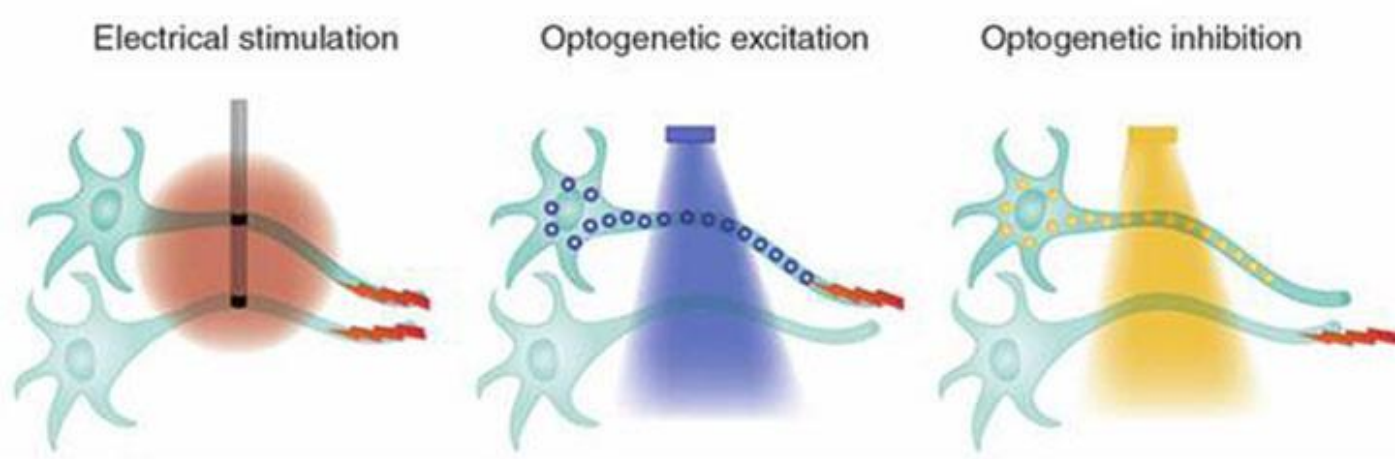
Channelrhodopsin

Halorhodopsin

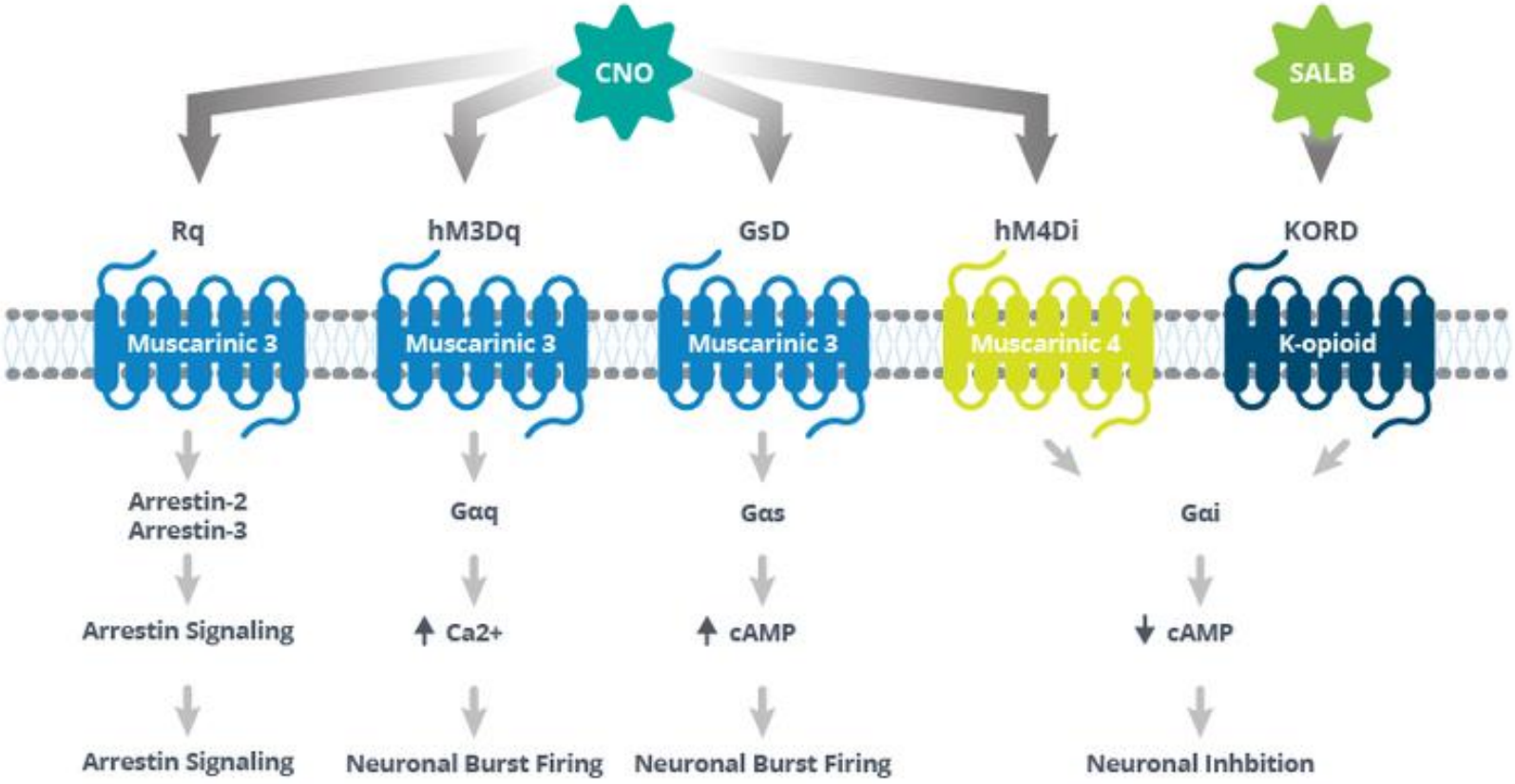


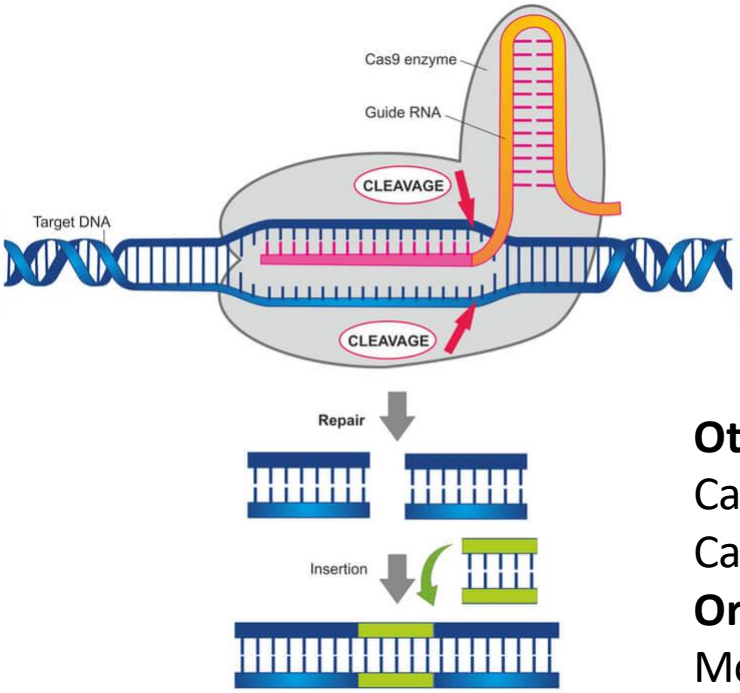
Bregestovski et al., 2016

Modulation of neuronal activity

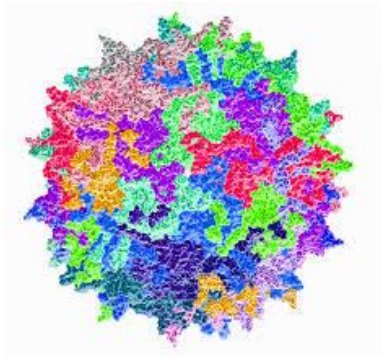


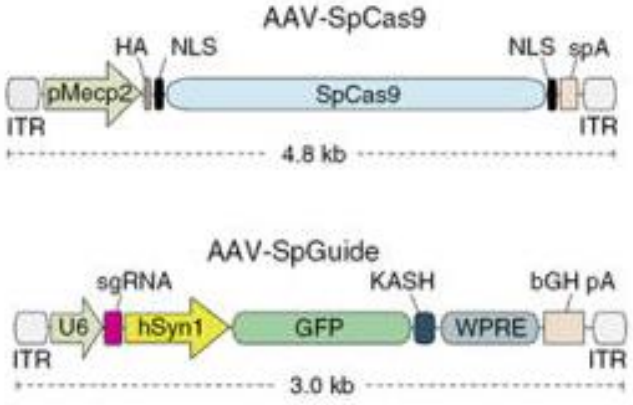
Chemogenetic
e.g. DREADD: Designer Receptors Exclusivelly Activated by Designer Drugs





Crispr/Cas9





Other approaches are possible to target RNA:

Cas 13

Cas7-11

Or non-coding DNA:

Modulators of chromatin organization

Gene activators

Limitations:

Off target cut

No reversibility on DNA, Slow reversibility on RNA

Other vehicles:

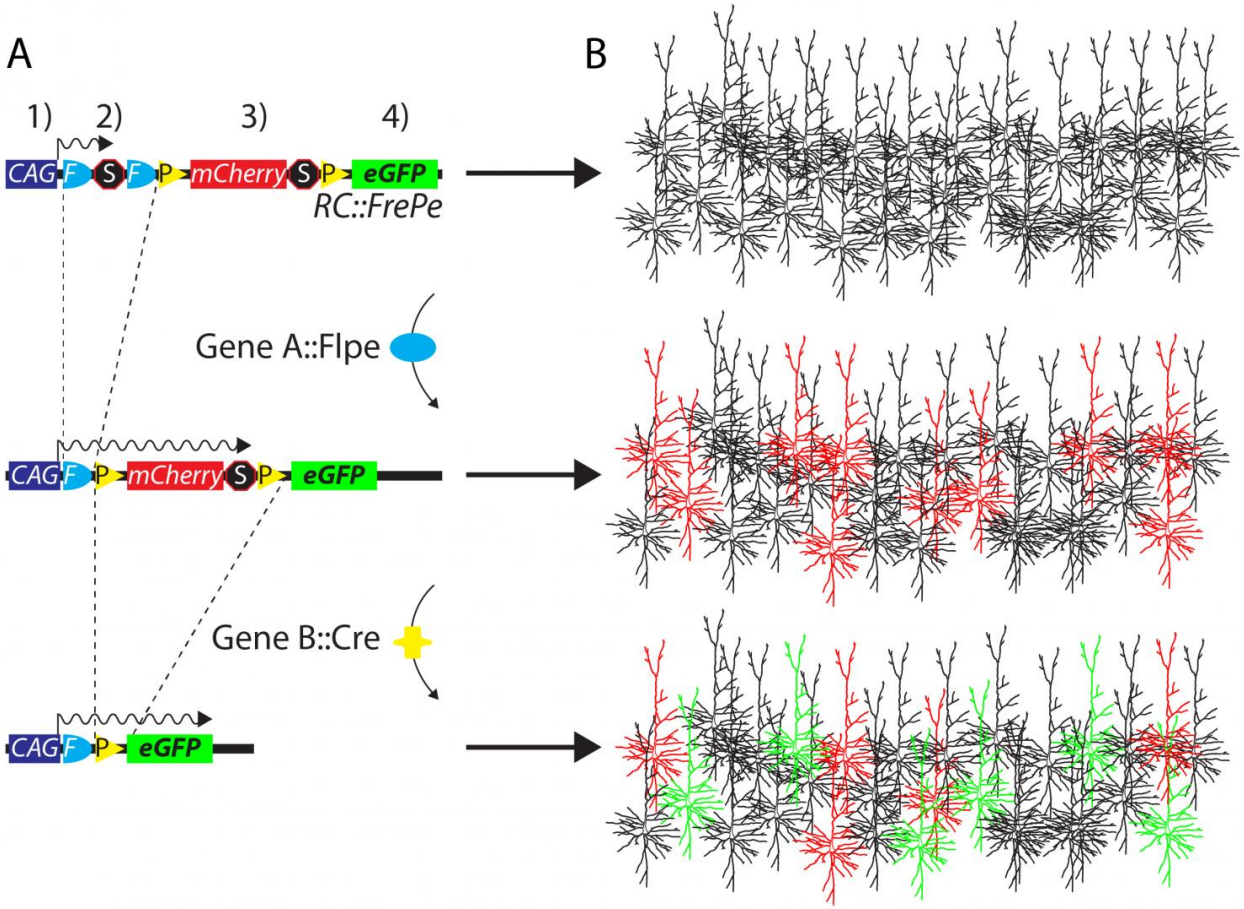
Adenovirus, Herpes, but AAV is the privileged one for humans

Delivery using lipid carriers or modified extracellular vesicle

Use of artificial nucleic acids to improve stability.


The
BrainXoup
Extra Full Synapses
PLUS FANTASY!
NEW EMOTIONS
is not a soup!
Conect Now
DORZBACH
Cake Brother Co - Since 2017
SERGIO L. FLECK

Intersectional Genetic



Russell Lab, Baylor College

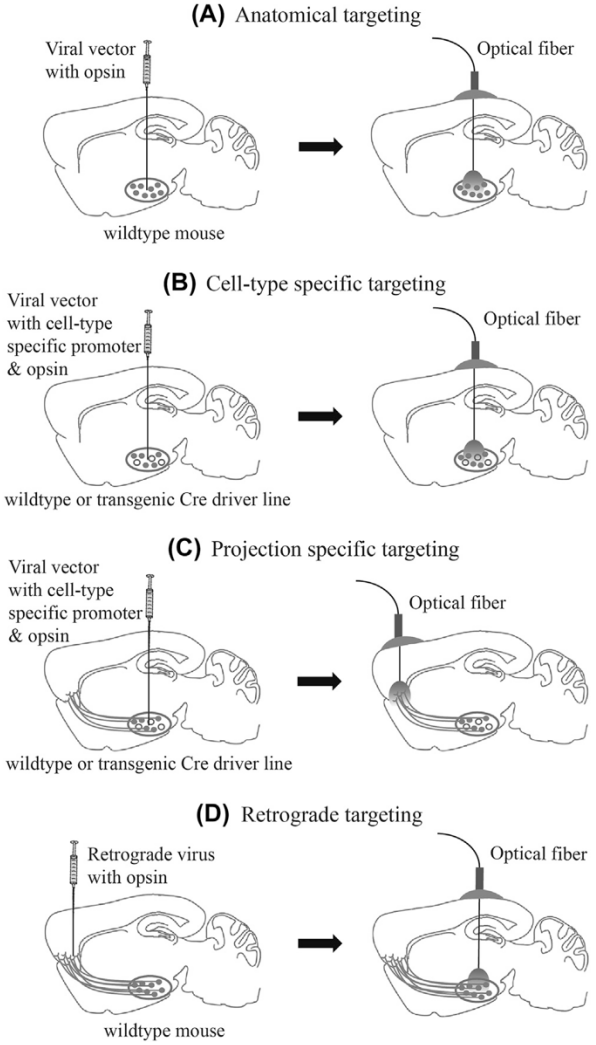
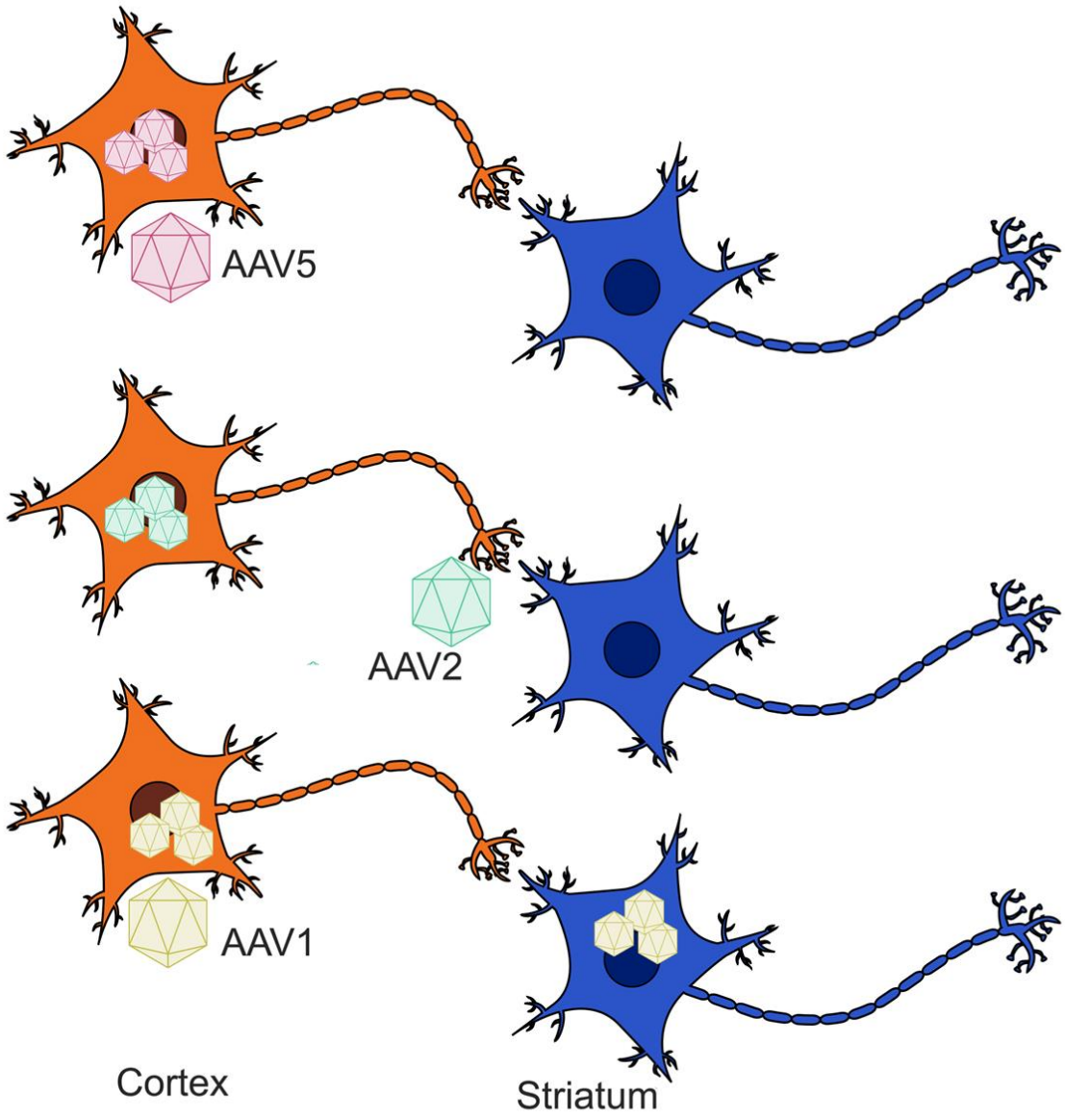


FIGURE 14.1 Targeting strategies using optogenetic tools. Schematic drawings of different targeting strategies for optogenetic manipulations in rodents. (A) Anatomical targeting. The optogenetic construct is delivered directly into the target brain region by stereotaxic injection of a viral vector (eg, adeno-associated virus or lentivirus) and the opsin is subsequently expressed in all cells (ie, neurons and glial cells) (left). The optical fiber is implanted above the target brain region (right). (B) Cell type–specific targeting. A viral vector carrying an optogenetic construct with a cell type–specific promoter will only infect genetically defined neurons (*filled circles*) but not other surrounding neurons (*open circles*) (left). The optical fiber is implanted directly above the viral injection site (right). An alternative approach is to use transgenic animals that express Cre recombinase in genetically defined neurons. (C) Projection targeting. A viral vector carrying a cell type–specific promoter and optogenetic construct is infused into the target brain region of a wild-type or transgenic mouse (left). The optical fiber is implanted above the brain region that contains axon terminals originating from the neurons in the viral injection site (right). (D) Retrograde targeting. A retrograde virus (eg, rabies virus) expressing an opsin is injected into a brain region which is innervated by neurons from a certain brain region (left). The optical fiber is implanted directly above this brain region and light stimulation will activate all neurons that project to the viral injection site (right).

Lammel et al., 2016

Playing with AAV serotypes



From tools to therapies?

Gene therapies and new pharmacology

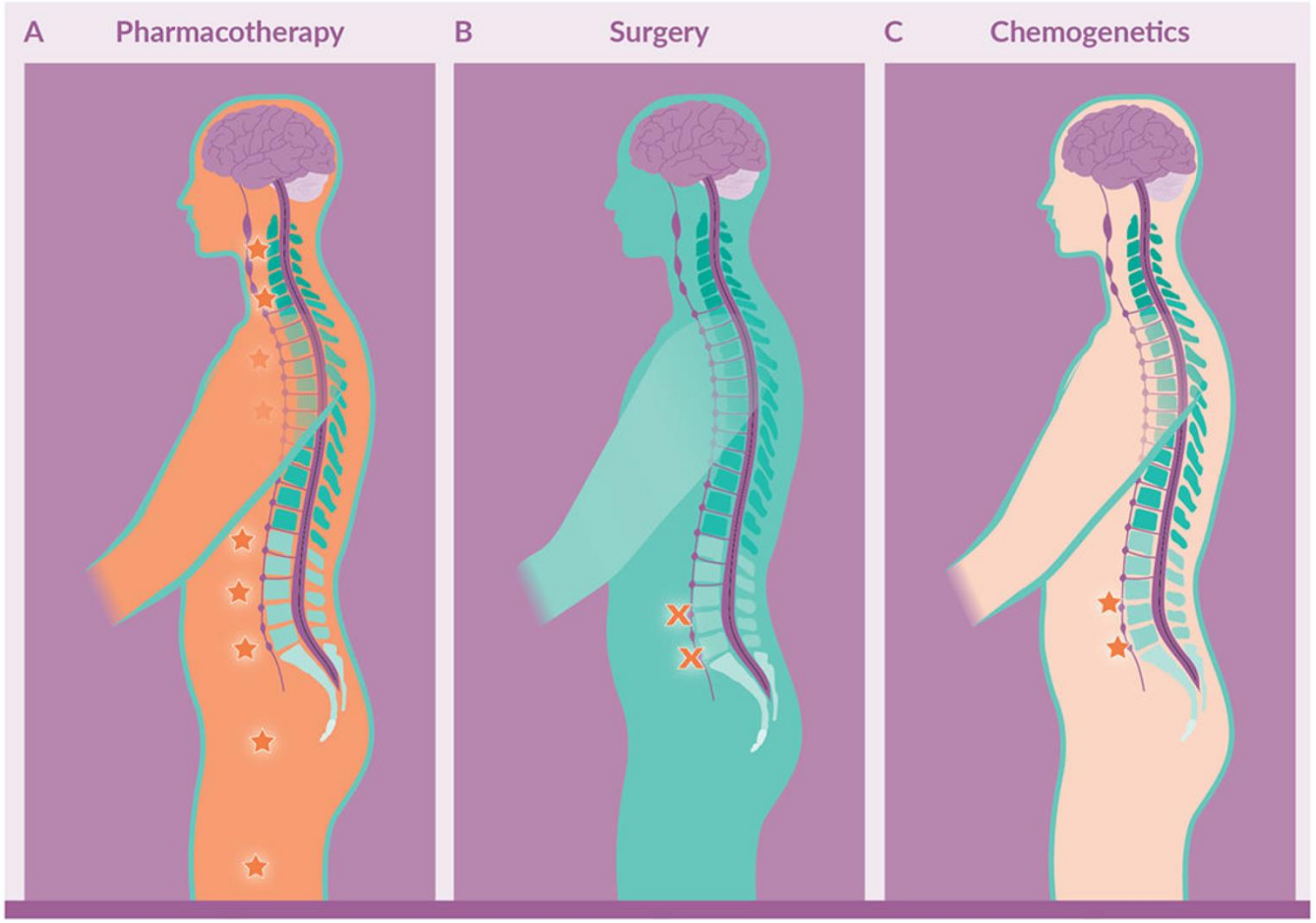


FIGURE 1. Three treatment approaches to nervous system therapy, example of chronic neuropathic pain.

Systemic pharmacotherapy results in widespread distribution of the drug (orange), which modulates (red stars) the affected sensory ganglia as well as all other sensory ganglia, the brain, and other peripheral organs that also express the target for the drug. Surgery procedures permanently disrupt the sensory ganglia (red x's) to block sensory transmission. Chemogenetics achieves local, tunable, and reversible neuromodulation by targeting a chemogenetic receptor solely to the neuropathic pain-causing ganglia. Ultrapotent chemogenetic receptors use low doses (light yellow) of the chemogenetic drug.