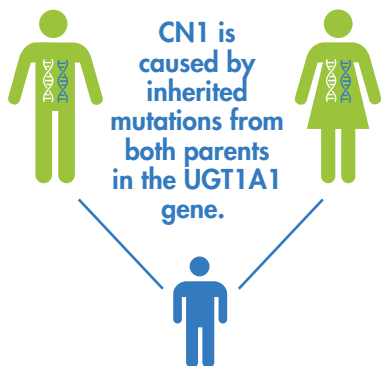


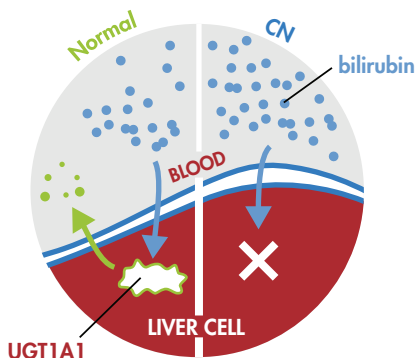
CRIGLER-NAJJAR AND THE POTENTIAL FOR GENE THERAPY



Crigler-Najjar Type 1 (CN1) is an ultra rare genetic disease that causes a build up of bilirubin in the blood.



Genetic mutations lower the activity of the UDP glucuronosyltransferase (UGT1A1) protein, which prevents the liver from breaking down and excreting bilirubin molecules, causing them to accumulate in the blood



Symptoms or Pathology include:

Kernicterus
(unconjugated bilirubin can cross the blood-brain barrier and therefore, patients with CN1 are at constant risk of developing severe, irreversible, neurological damage, which can lead to death)

Severe Jaundice
(yellowing of the skin)

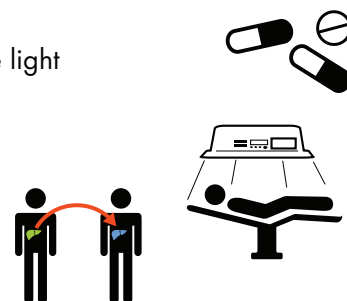
extremely high levels of bilirubin in the liver

Current treatments have limitations

Phototherapy:
10-12 hours a day under blue light

Some patients respond to phenobarbital

Liver transplant:
Limited availability, high risk

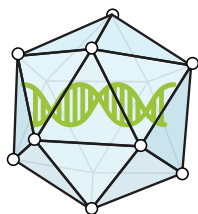


MIGHT GENE THERAPY HELP CRIGLER-NAJJAR PATIENTS?

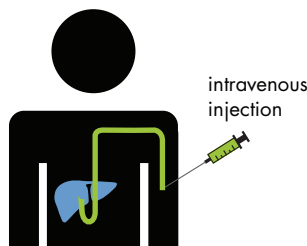
This promising new experimental therapy strives to overcome the patient's genetic mutation by delivering a healthy copy of the UGT1A1 gene to the liver.



1. a normal healthy copy of the UGT1A1 gene is produced



2. gene is inserted into a harmless Adeno-Associated Virus (AAV) to create a viral vector



3. AAV vector is delivered to the patient's vein, sending it to the liver



4. liver cells (hepatocytes) take up vector and begin to express functional UGT1A1



5. functional UGT1A1 can convert unconjugated bilirubin to conjugated bilirubin, lowering blood total bilirubin levels

One-time treatment

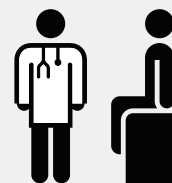
gene therapy has the potential to last for many years

Safety First



gene therapy has proven relatively safe and effective in animal models of Crigler-Najjar

What's next?



- the same vector has shown promise in patients with Hemophilia
- early clinical trials are under way to test the safety of this promising new therapy in patients with Crigler-Najjar