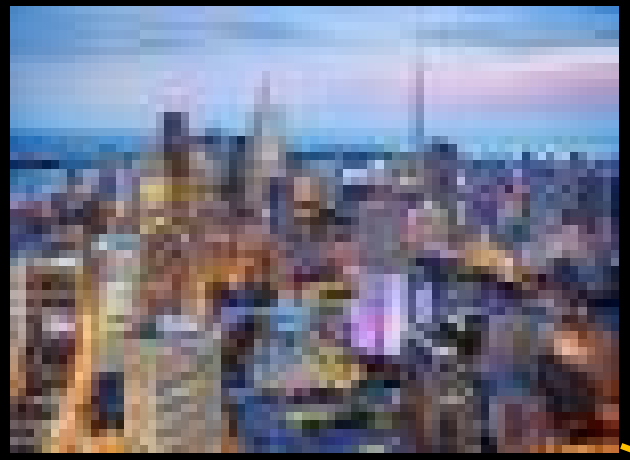
Huntington's Disease Education Day

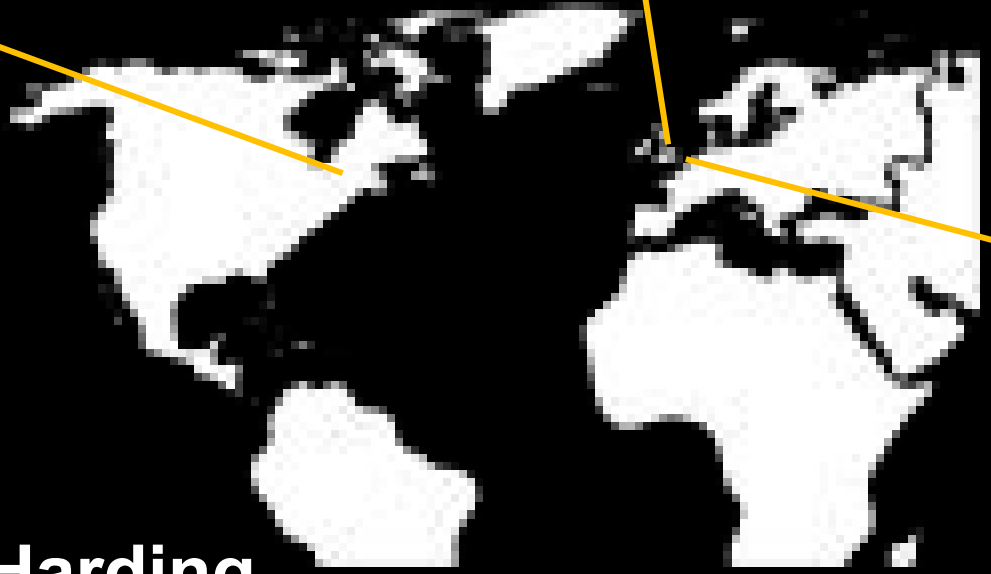
HDSA Centre of Excellence
University of Washington, Tacoma

HD BUZZ



Postdoctoral fellowship and independent research career, Toronto, Canada

Undergraduate and PhD Oxford, U.K.



Hometown Dover, U.K.

Rachel Harding

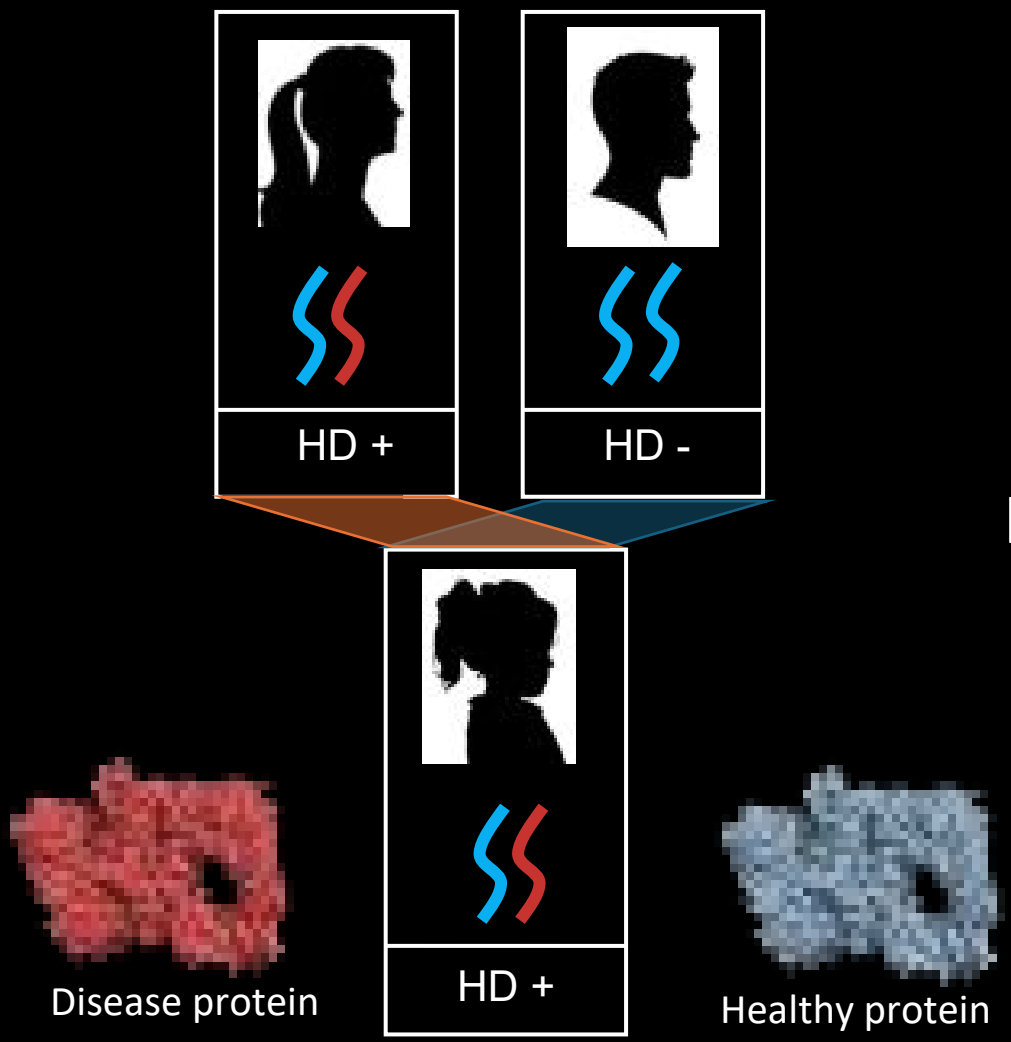
Co-Editor-in-Chief HDBuzz

Assistant Professor, University of Toronto

Harding Lab at University of Toronto

The Harding lab consists of 12 researchers, all of whom are dedicated to HD research.

We investigate the huntingtin protein and how it is changed in HD and explore new avenues of drug discovery for HD and related diseases.



We have two copies or alleles of the HTT gene

People with HD make two types of the HTT protein in every cell of their bodies:

the **disease** and **healthy** forms

Unexpanded
HTT gene

…CTCAAGTCCTTCCAGCAGCAGCAGCAGCAGCA
GCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCA
GCAGCAGCAGCAACAGCCGCCACCGCCG…

10-26 repeats is typical

27-35 repeats means your children may develop HD
36-39 repeats means you may develop HD

Expanded
HTT gene

…CTCAAGTCCTTCCAGCAGCAGCAGCAGCAGCA
GCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCA
GCAGCAGCAGCAACAGCAGCAGCAGCAGCAGCA
GCAGCAGCAGCAACAGCAGCAGCAGCAGCAGCA
GCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCA
GCAGCAGCAGCAGCAACAGCCGCCACCGCCG…

40+ leads to HD

Unexpanded
HTT gene

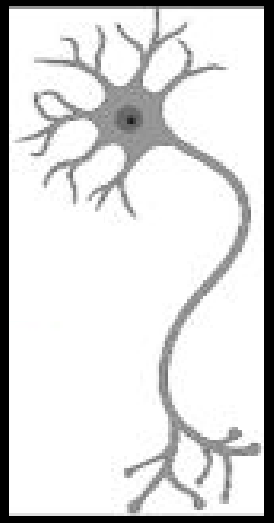
Regular
wildtype HTT
protein

Healthy nerve cells

Expanded
HTT gene

Expanded
HTT
protein

Sick nerve cells



RH

Other genes can influence when symptoms of HD might begin

Same CAG length

Symptoms **earlier** in life

Symptoms **later** in life

Cell

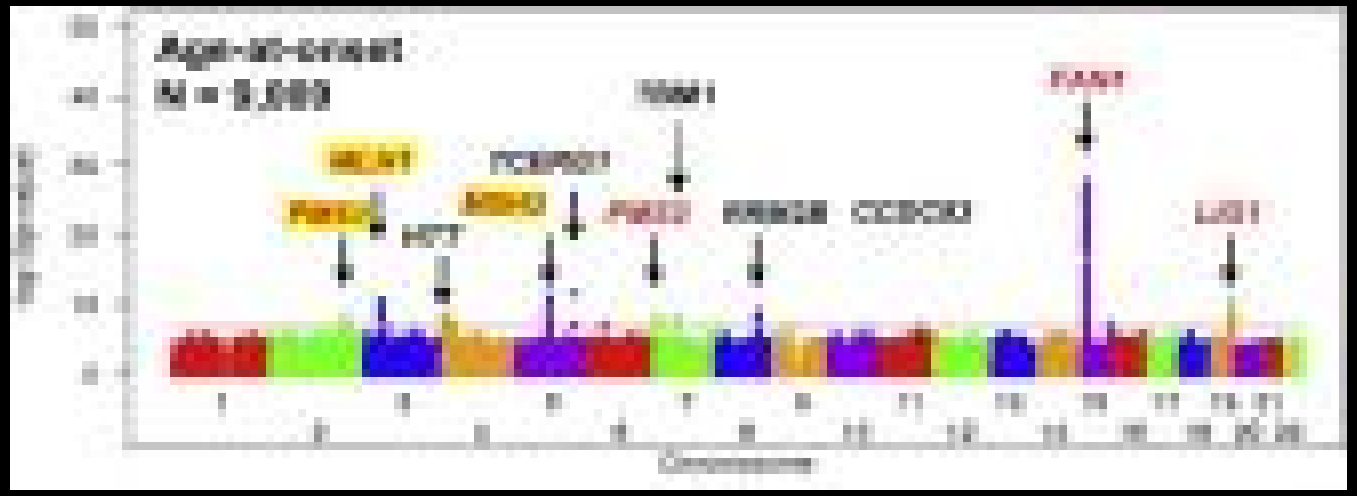
Volume 162, Issue 3, 30 July 2015, Pages 516-526

Article

Identification of Genetic Factors that Modify Clinical Onset of Huntington's Disease

Genetic Modifiers of Huntington's Disease (GeM-HD) Consortium[&,88]

Many genetic modifiers of HD map to genes involved in DNA repair



Lots of research is underway to figure out exactly why these modifiers change when symptoms start

A leading theory is that some of these genes alter a process called somatic instability

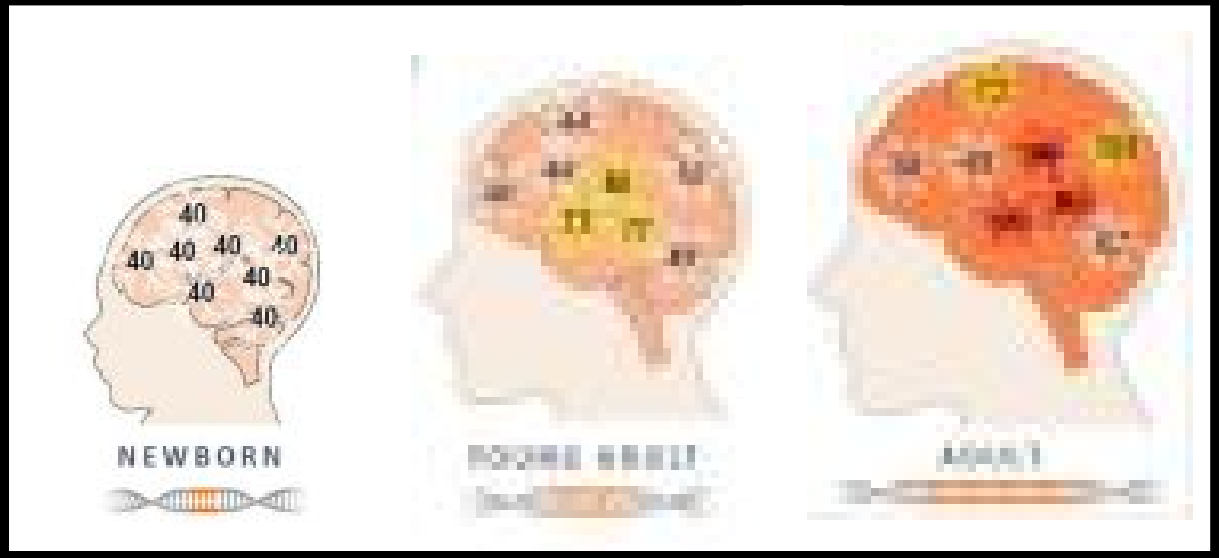
In some cells, the CAG number gets bigger over time

HTT gene

Most cells

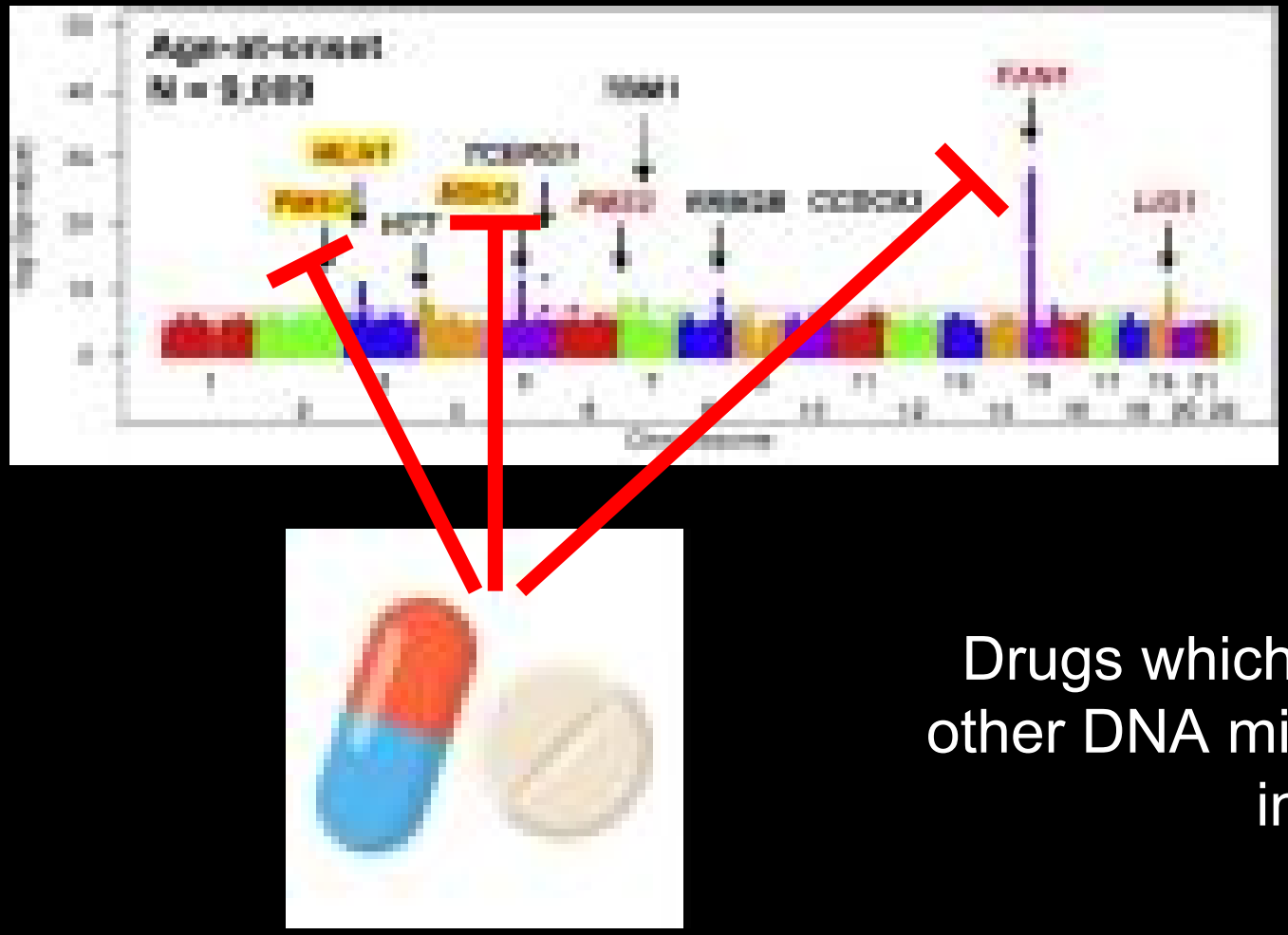
Some brain cells

DNA repair gone wrong



Lots of HD scientists are busy trying to figure out how somatic expansion contributes to how HD works

Genetic modifiers of HD could be good drug targets



Slowing down somatic expansion might slow down HD

Drugs which target MSH3, FAN1 and other DNA mismatch repair proteins are in development

Many companies are pursuing somatic expansion as a target for HD therapies

HDBUZZ

Loqus23 THERAPEUTICS

HARNESS THERAPEUTICS

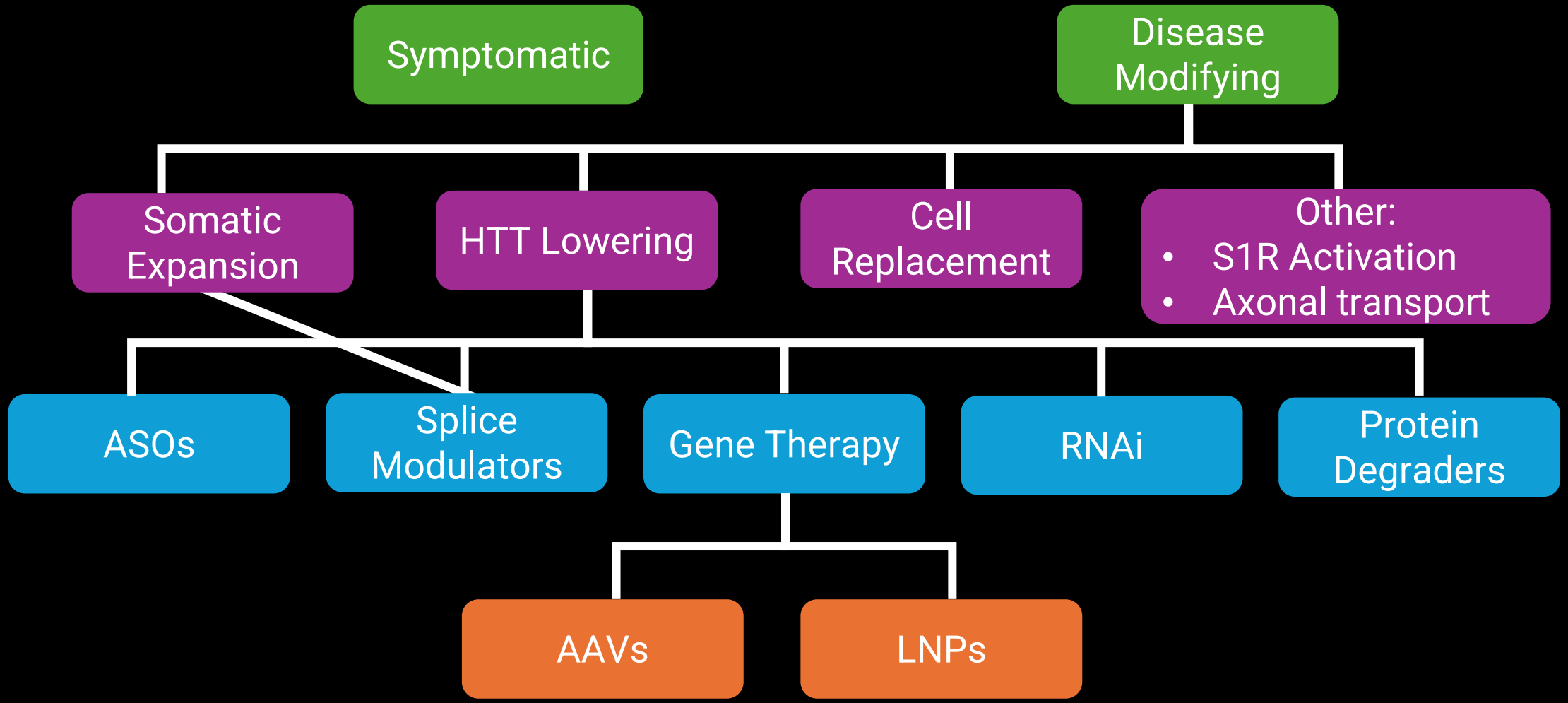
Latus

REVIR Therapeutics

Pfizer

Rgenta

Current strategies to try to treat HD



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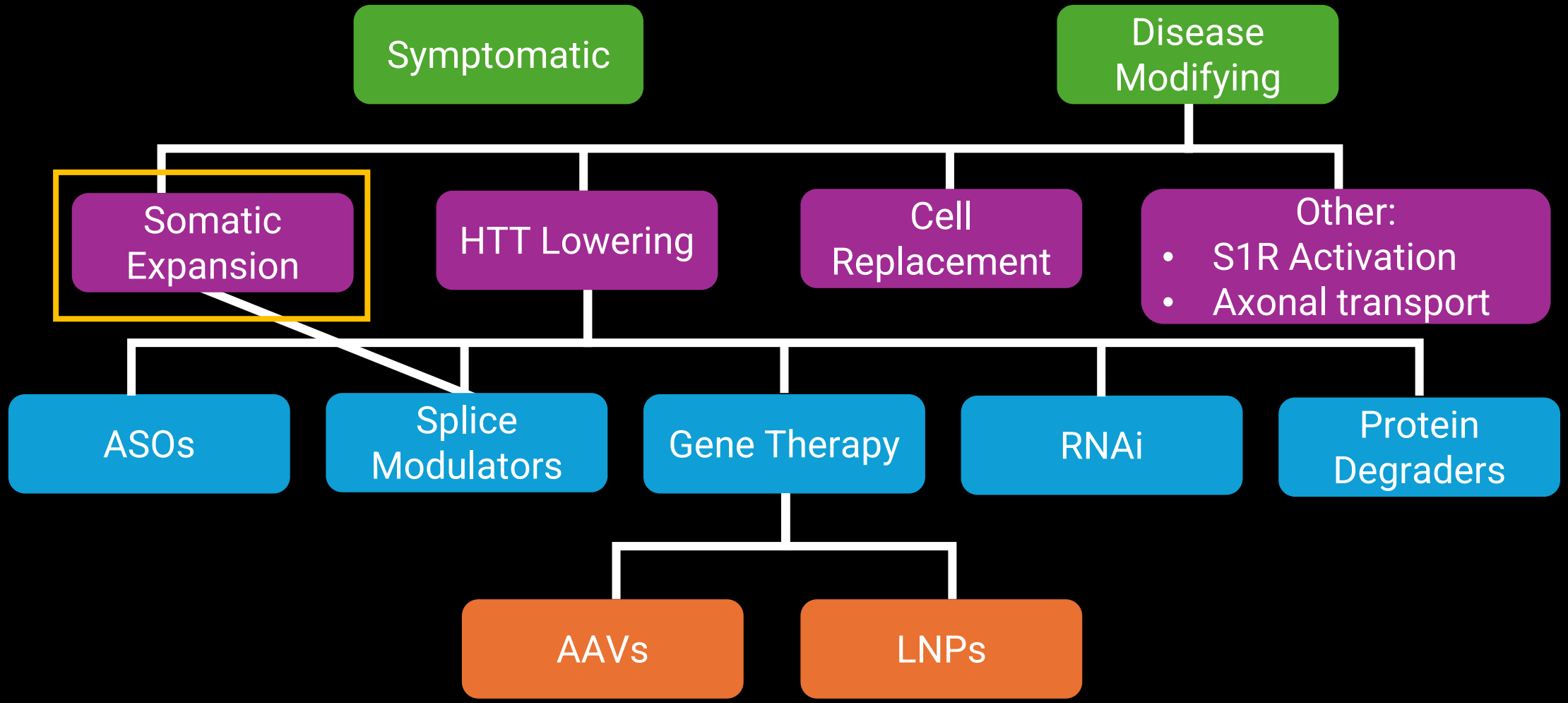
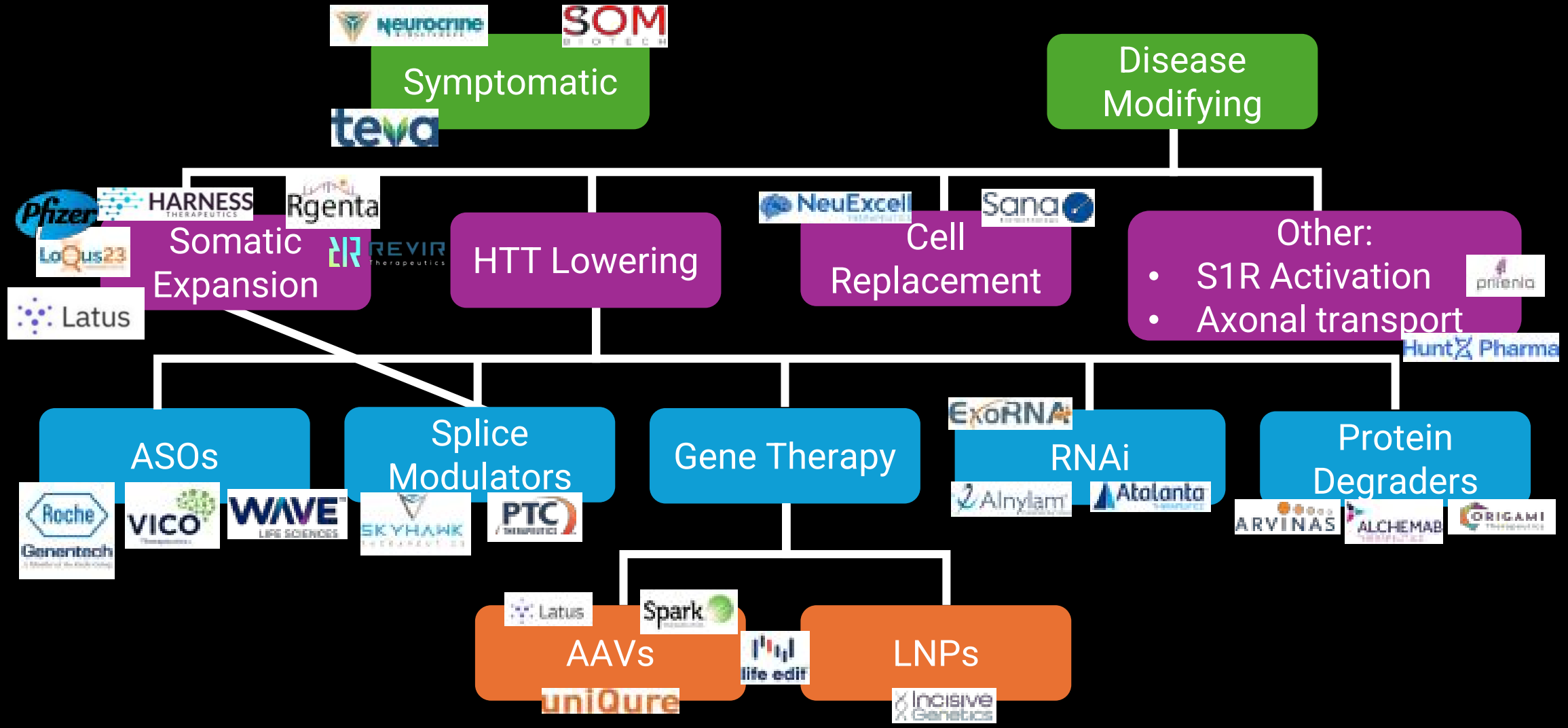
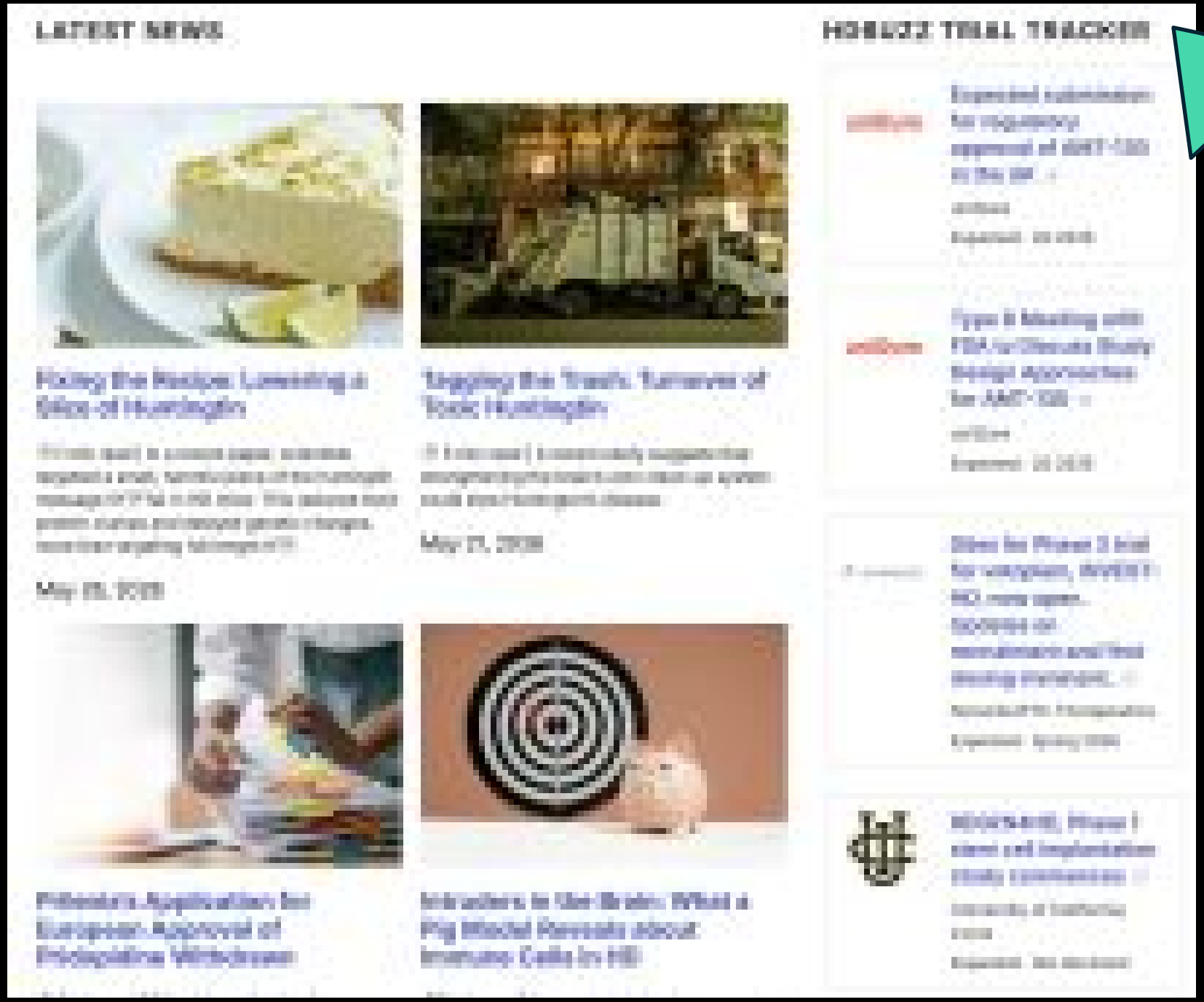


Companies in or heading to the clinic





Find out when to expect updates on clinical trials

Companies in or heading to the clinic