

**HD BUZZ**

**Huntington's Disease  
Education Day**

**HDSA Centre of Excellence  
University of Washington, Tacoma**

# HO

# BUZZ

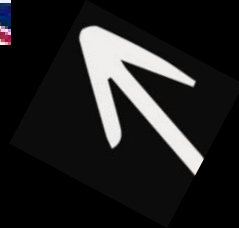




Postdoctoral  
fellowship and  
independent  
research career,  
Toronto, Canada



Undergraduate and PhD  
Oxford, U.K.



**Rachel Harding**  
Co-Editor-in-Chief HDBuzz  
Assistant Professor, University of Toronto



Hometown  
Dover, U.K.



# 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.

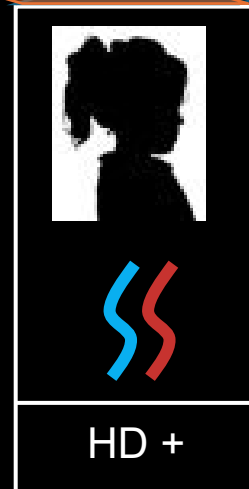
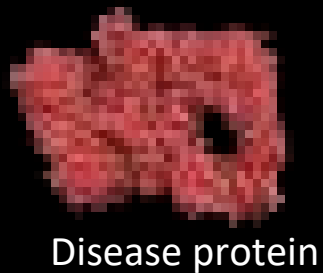




We have two copies or alleles of the HTT gene

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

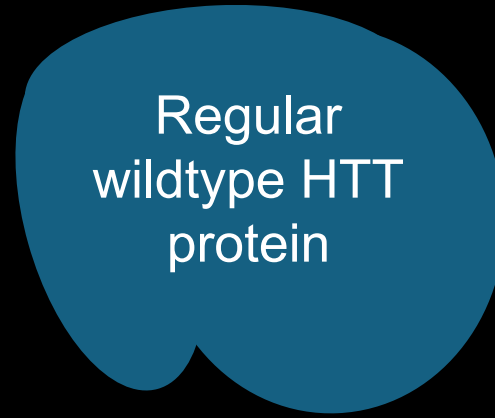


...CTCAAGTCCTTCCAGCAGCAGCAGCAGCAGCA  
GCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCA  
GCAGCAGCAGCAACAGCAGCAGCAGCAGCAGCA  
GCAGCAGCAGCAACAGCAGCAGCAGCAGCAGCA  
GCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCA  
GCAGCAGCAGCAGCAACAGCCGCCACCGCCG...

40+ leads to HD



Unexpanded  
HTT gene



Regular  
wildtype HTT  
protein

Healthy nerve cells

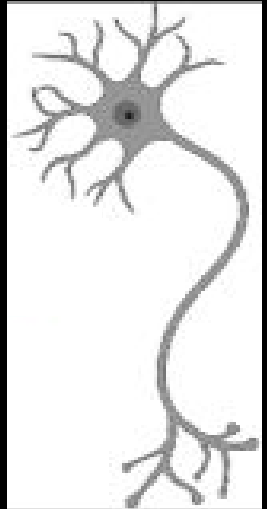


Expanded  
HTT gene



Expanded  
HTT  
protein

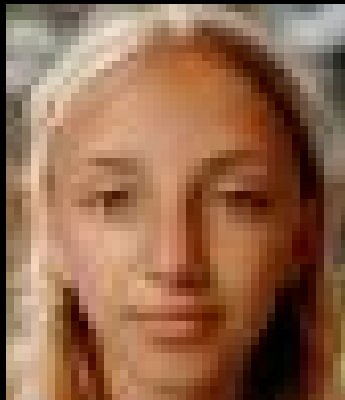
Sick nerve cells



# Other genes can influence when symptoms of HD might begin



Same CAG length



Symptoms **earlier** in life



Symptoms **later** in life

**Cell**

CellPress

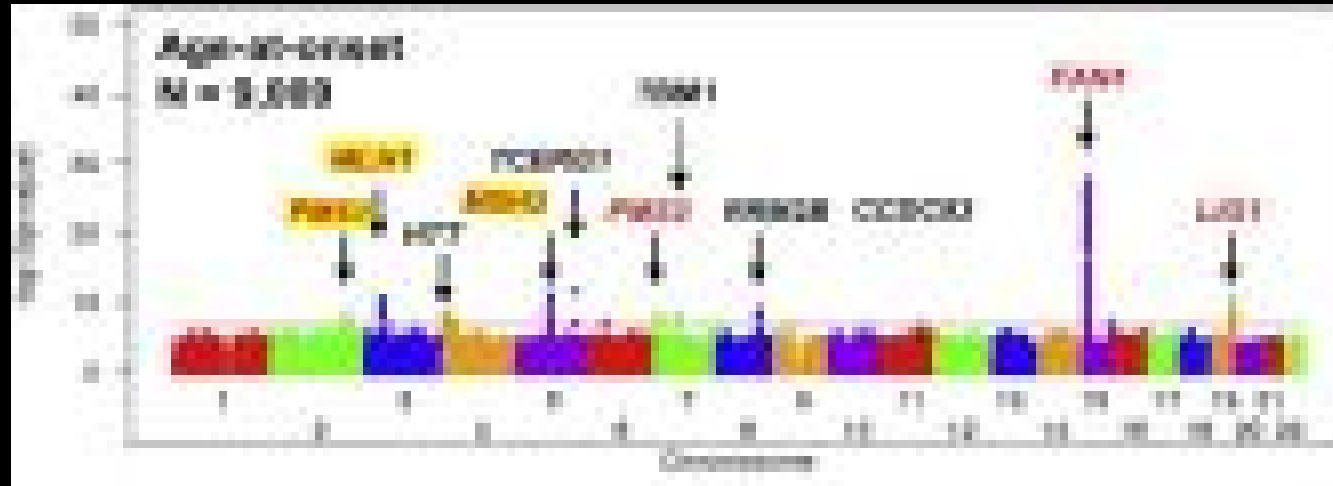
Volume 162, Issue 3, 30 July 2015, Pages 518-526

Article

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

Genetic Modifiers of Huntington's Disease (GeM-HD) Consortium<sup>1,2</sup>

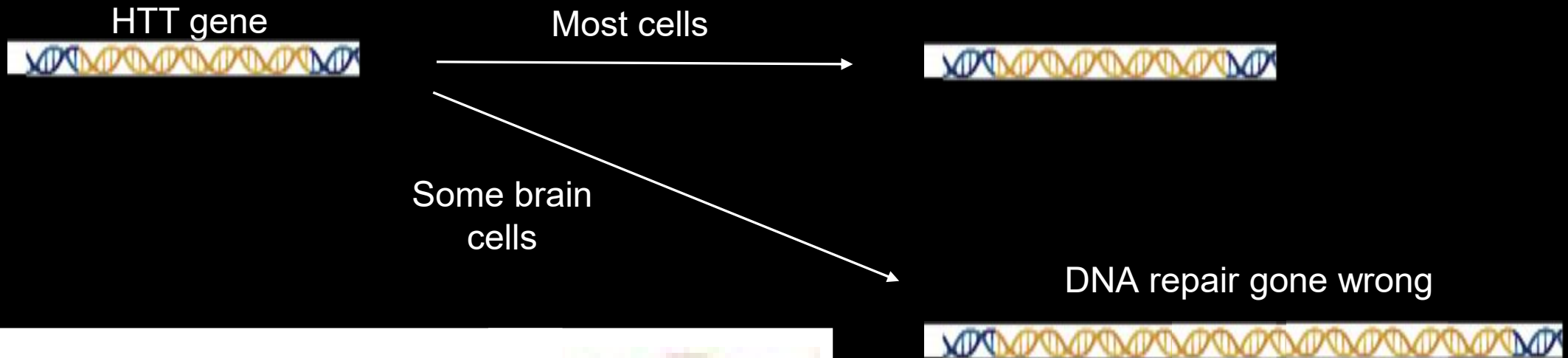
# Many genetic modifiers of HD map to genes involved in DNA repair



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



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

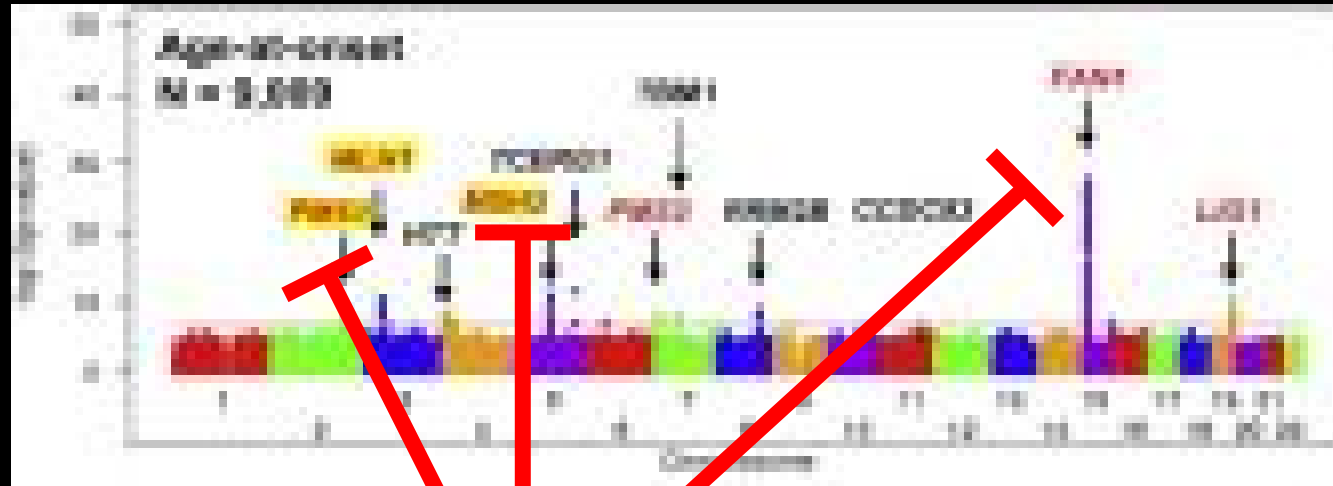


The screenshot shows the HD Buzz website. At the top left is the HD Buzz logo with the tagline "Huntington's Disease Research News, Updates, Insights, and More for the global HD community". The navigation bar includes "Home", "About", "Contact", "Subscribe", and "Log Out".

The main content area features two articles:

- Left Article:** "The latest volume of HD genetics research reveals new gems but also mysteries". The text below the title states: "Each year, our HD genetics journal publishes new research on HD genetics. Scientists have revealed the most in a series of genetic studies examining the genetic changes, which might be key parts to develop treatments for HD." The author is "By Tom Skovron" and the date is "April 28, 2023".
- Right Article:** "Stopping C-A-G Repeat Expansion in Its Tracks". The text below the title states: "A new study shows that lowering MMR1, a key DNA repair protein, with antisense oligonucleotides (ASOs) can stop CAG repeat expansion in HD patient-derived cells. This could be a promising way to slow symptom onset and progression." The author is "By Dr. Thomas Cross" and the date is "April 24, 2023".

# Genetic modifiers of HD could be good drug targets

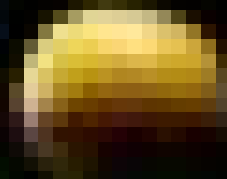
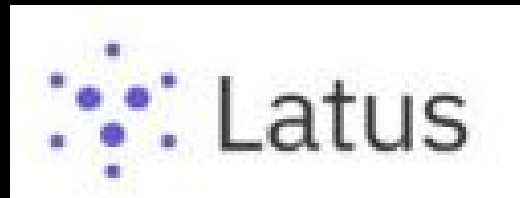


Slowing down somatic expansion might slow down HD

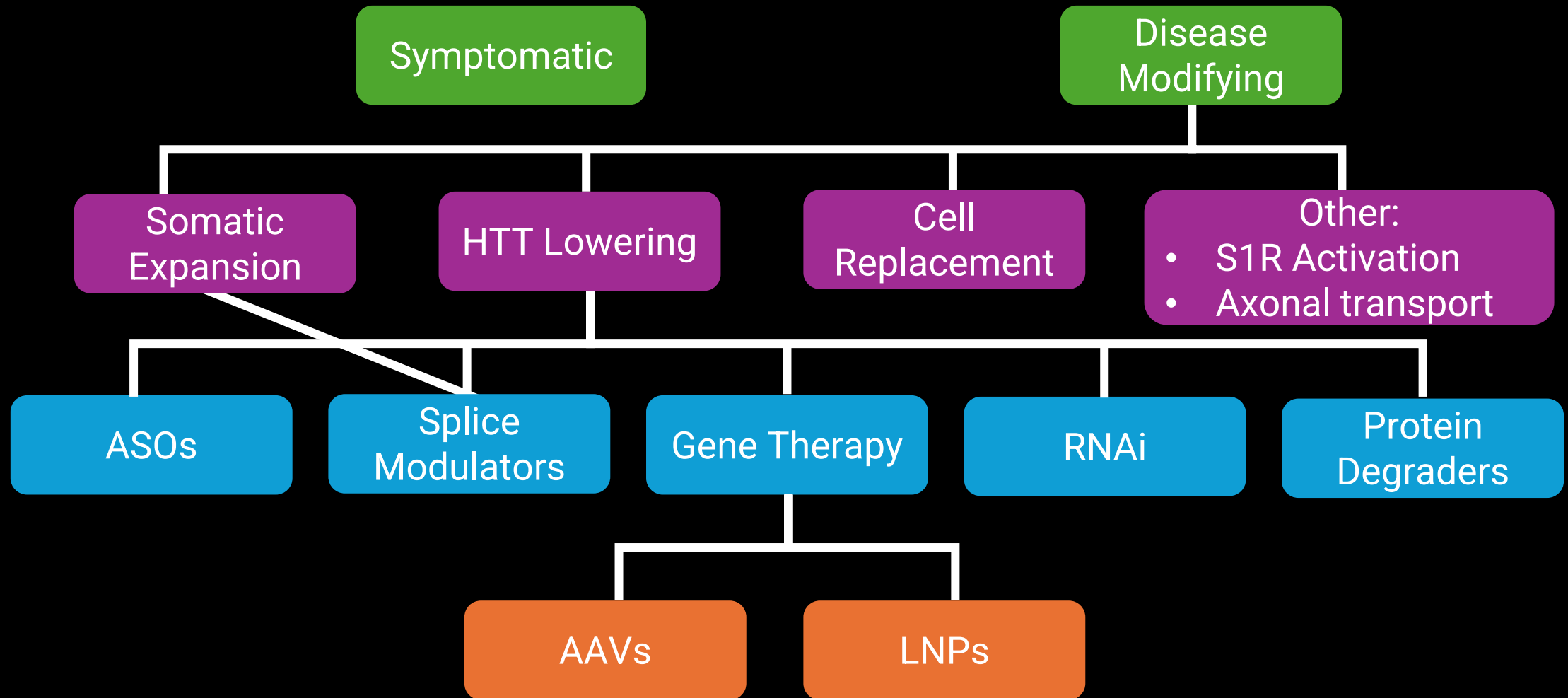


Drugs which target MSH3, FAN1 and other DNA mismatch repair proteins are in development

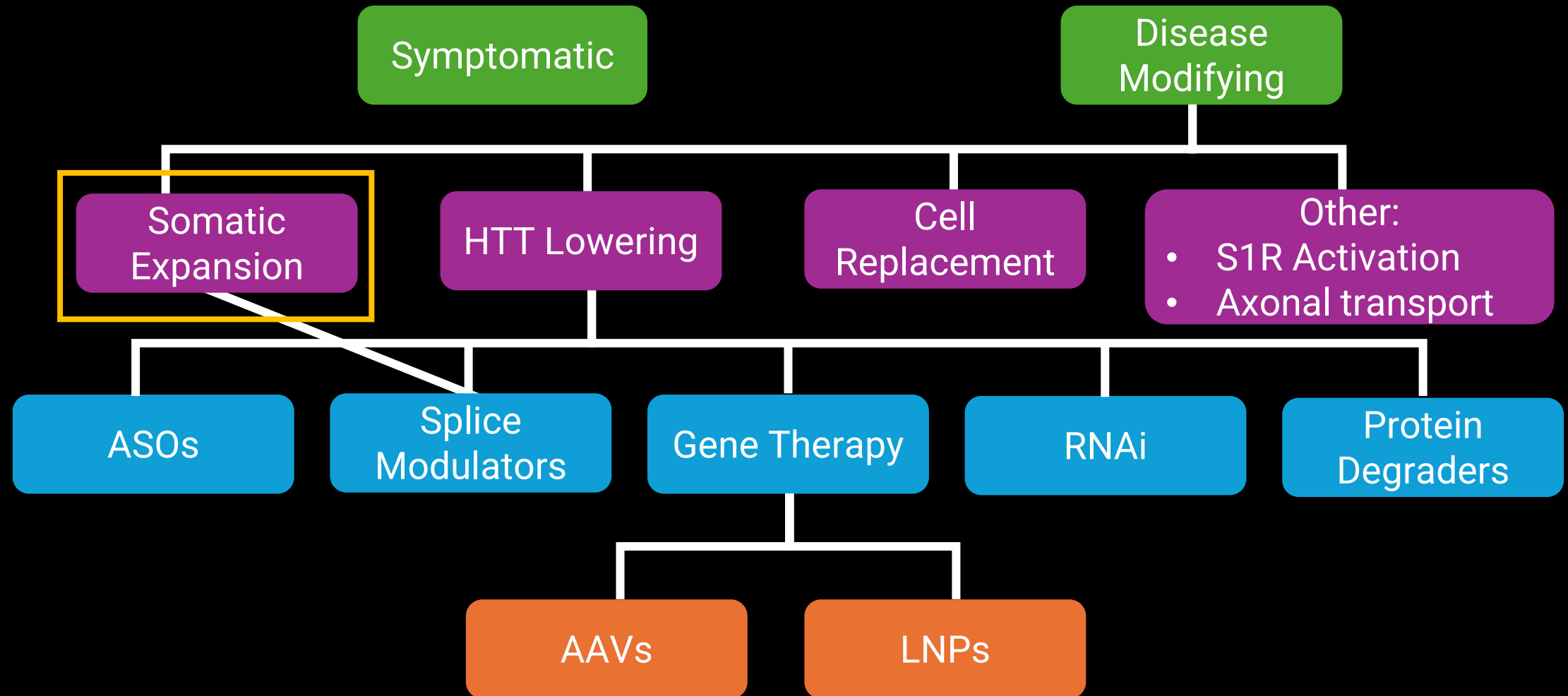
Many companies are pursuing somatic expansion as a target for HD therapies



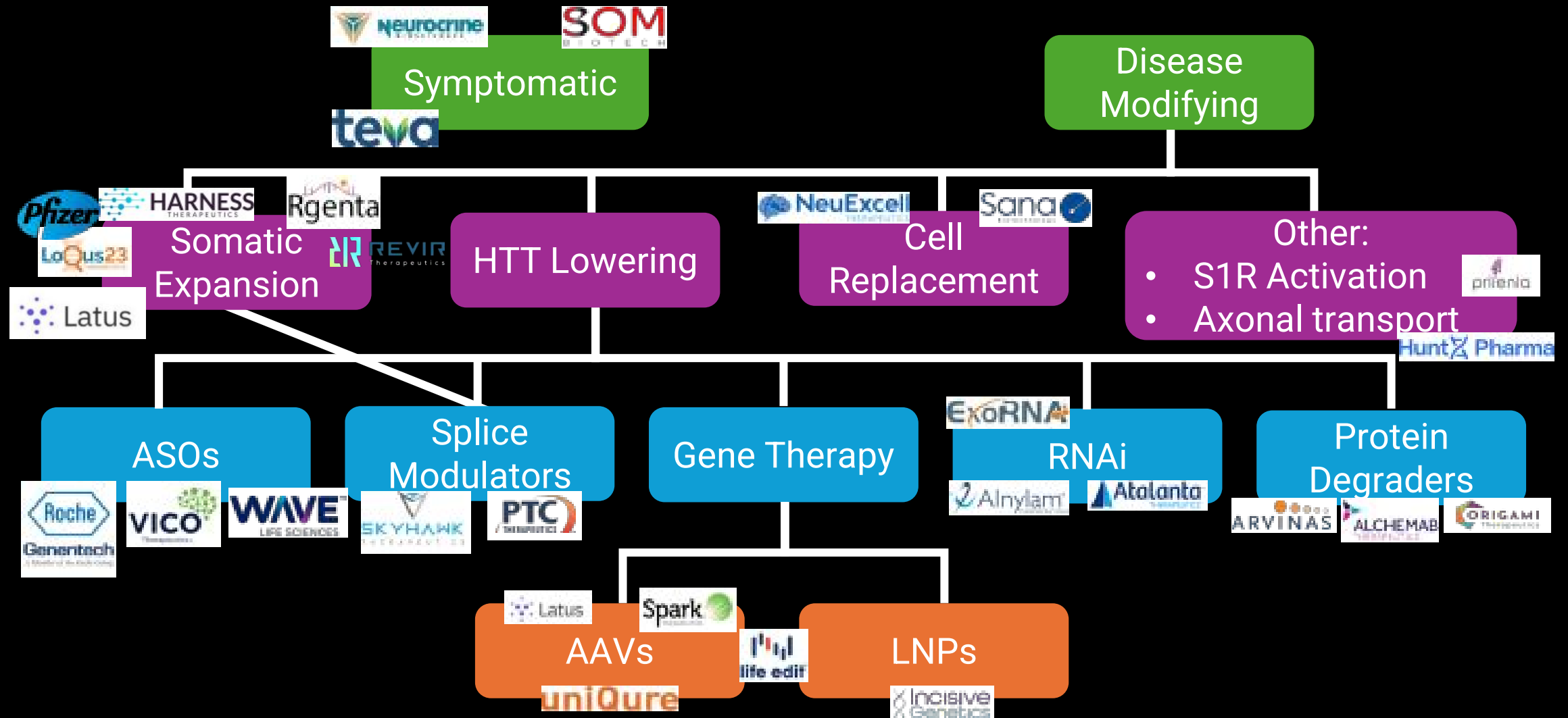
# Current strategies to try to treat HD



# Current strategies to try to treat HD



# Companies in or heading to the clinic



## LATEST NEWS



### Following the Recipe: Launching a Slice of Huntington

From seed to harvest, science supports and sustains our economic success. With a new day, this sector has great future potential. Learn how to get started by following the recipe.

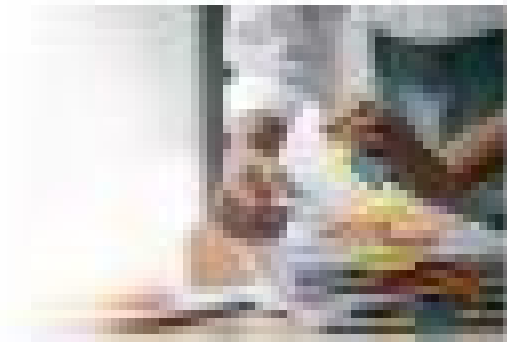
May 18, 2018



### Tagging the Trees: Turnover of Toxic Huntington

It's time to turn over a new leaf. Learn how to get started by following the recipe.

May 17, 2018



### Patent Applications for European Approval of Intrathecal Vincristine



### Intrathecal in the Brain: What a Pig Model Reveals about Immature Cells in MS

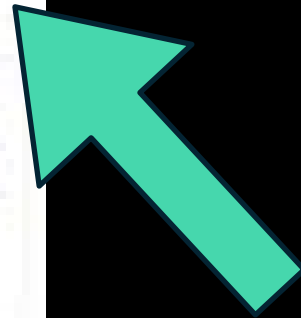
## HOBUST: TRIAL TRACKER

**Expected submission for regulatory approval of AMT-1300 to the FDA**  
AMT-1300  
Expected: 2018

**Type II Meeting with FDA regarding Study Design Approaches for AMT-1300**  
AMT-1300  
Expected: 2018

**Open for Phase II trial for relapsing, RRMS in the US**  
AMT-1300  
Expected: 2018

**Abstract, Phase I study and implementation study submitted**  
AMT-1300  
Expected: 2018



Find out when to expect updates on clinical trials

# Companies in or heading to the clinic

