# Tyrosine degradation through NTBC-resistant gene therapy

**HT1 Patient**

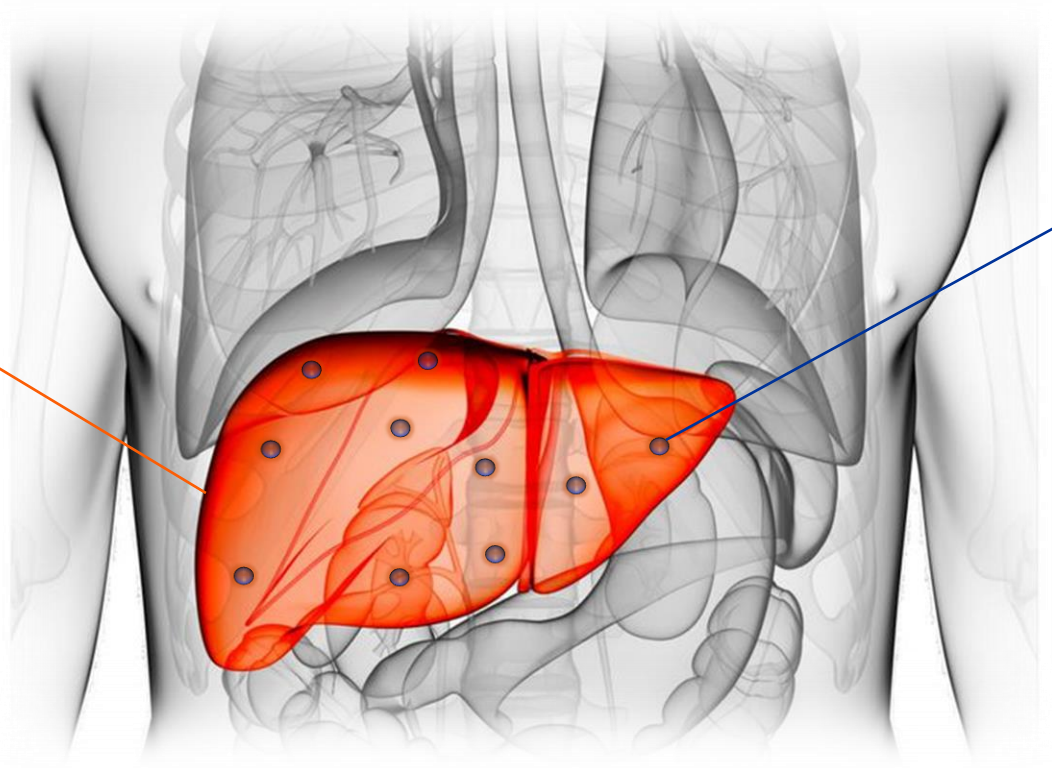
**Traditional HT1 treatment**

Defective FAH

All cells sensitive to NTBC treatment

= OK, but treatment blocks tyrosine degradation in all cells

→Dietary tyrosine restriction necessary



**Improved HT1 treatment**
*NTBC + AAV therapy*

Introduce FAH + NTBC-insensitive HPD ($HPD^{\Delta NTBC}$) through AAV gene therapy in 5-10% hepatocytes

= Restoration of tyrosine degradation in 5-10% of hepatocytes → sufficient to control normal dietary tyrosine intake

Unmodified cells remain sensitive to ongoing NTBC treatment

***TREATMENT***
***NTBC***
***restricted diet***

***TREATMENT***
***NTBC***
***+ AAV-FAH-HPD$^{\Delta NTBC}$***

***Normal diet***

# Tyrosine degradation through NTBC-resistant probiotics

## HT1 Patient

**Traditional HT1 treatment**

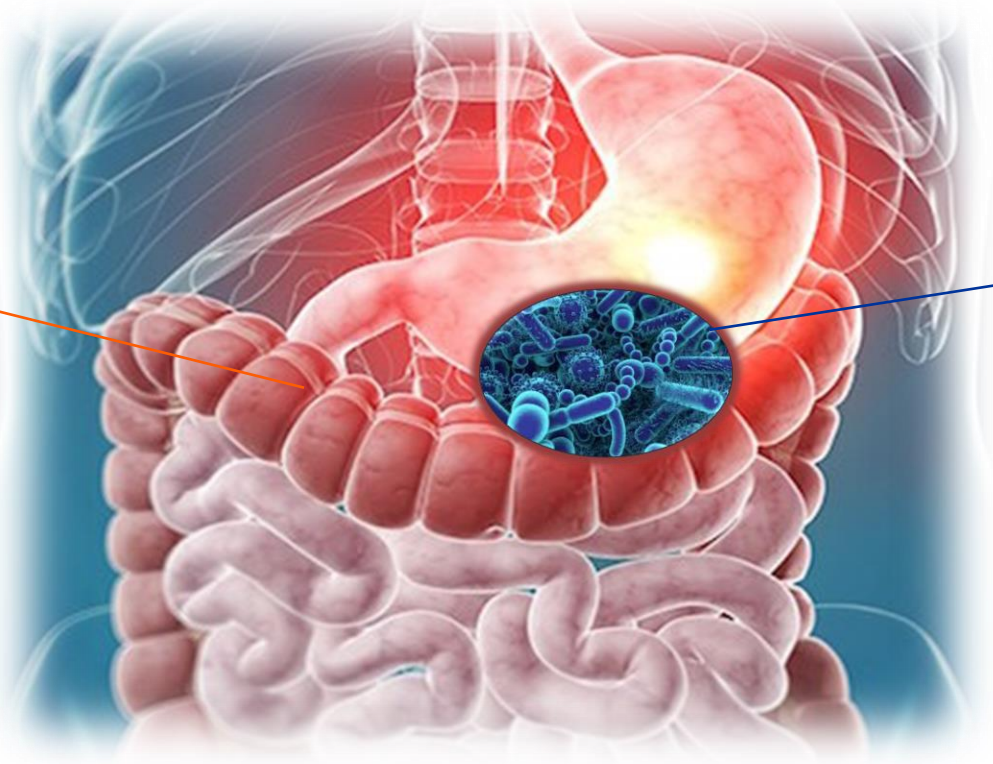
Defective FAH

All cells sensitive to NTBC treatment including micro-organisms in gut

= OK, but treatment blocks tyrosine degradation in all cells (host+microbiome)

→Dietary tyrosine restriction necessary

***TREATMENT***
***NTBC***
***restricted diet***



**Improved HT1 treatment**
*NTBC + oral probiotic*

Genetically engineered probiotic expressing NTBC-insensitive HPD enzyme ($HPD^{\Delta NTBC}$)

= Restoration of tyrosine degradation in gut

= Elimination of excess tyrosine through the gut

Human cells remain sensitive to ongoing NTBC treatment

***TREATMENT***
***NTBC***
***Probiotics-HPD$^{\Delta NTBC}$***

***Normal diet***