How cells proofread genetic messages

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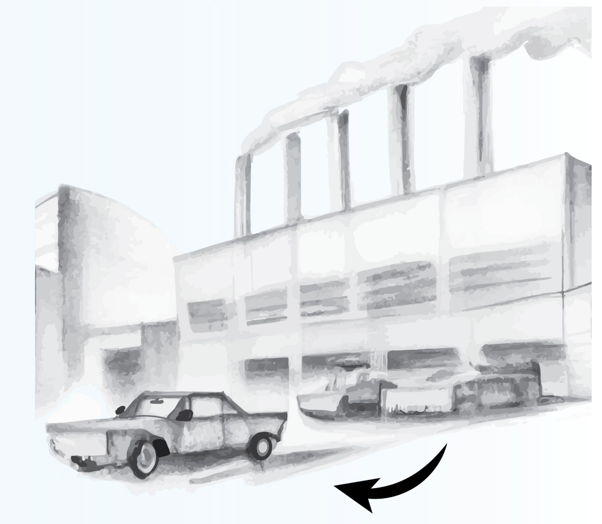
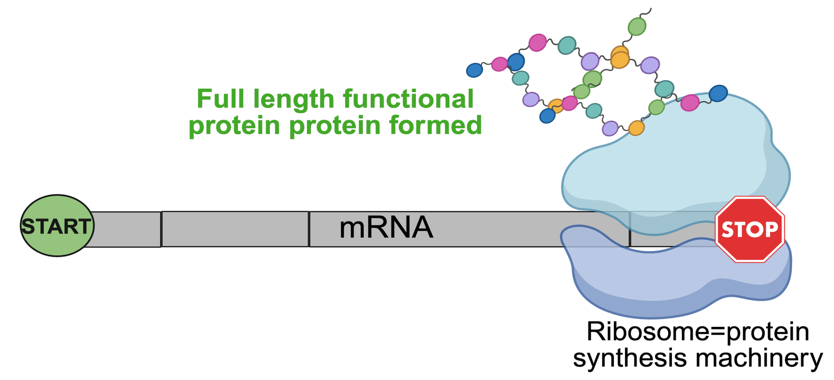
A surveillance mechanism that eliminates faulty messenger RNAs



mRNA = Blueprint that carries instructions to make a **protein**

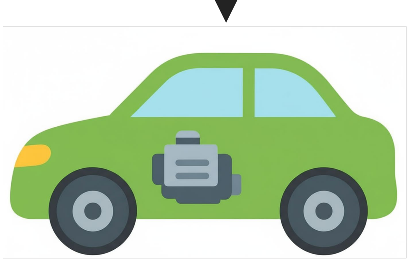
A car factory receives a blueprint:

Chassis → engine → wheels → paint the car green



Normal Blueprint

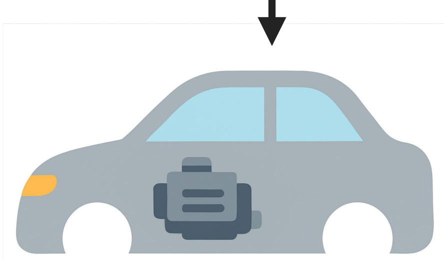
Chassis → engine → wheels → paint the car green



Complete and functional car

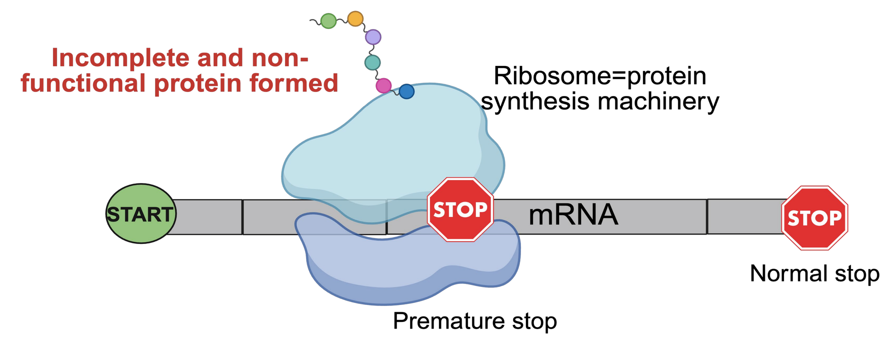
Faulty Blueprint

Chassis → engine → **STOP**

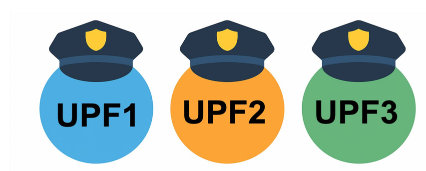


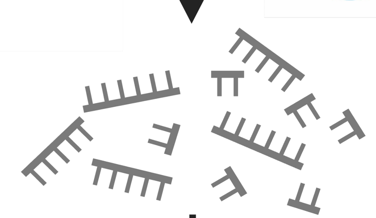
Incomplete and defective car

Limited by quality control

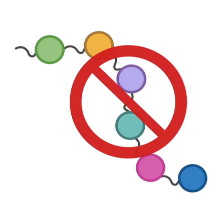


Faulty mRNAs (messages) are recognized by the three **UPF** Inspectors



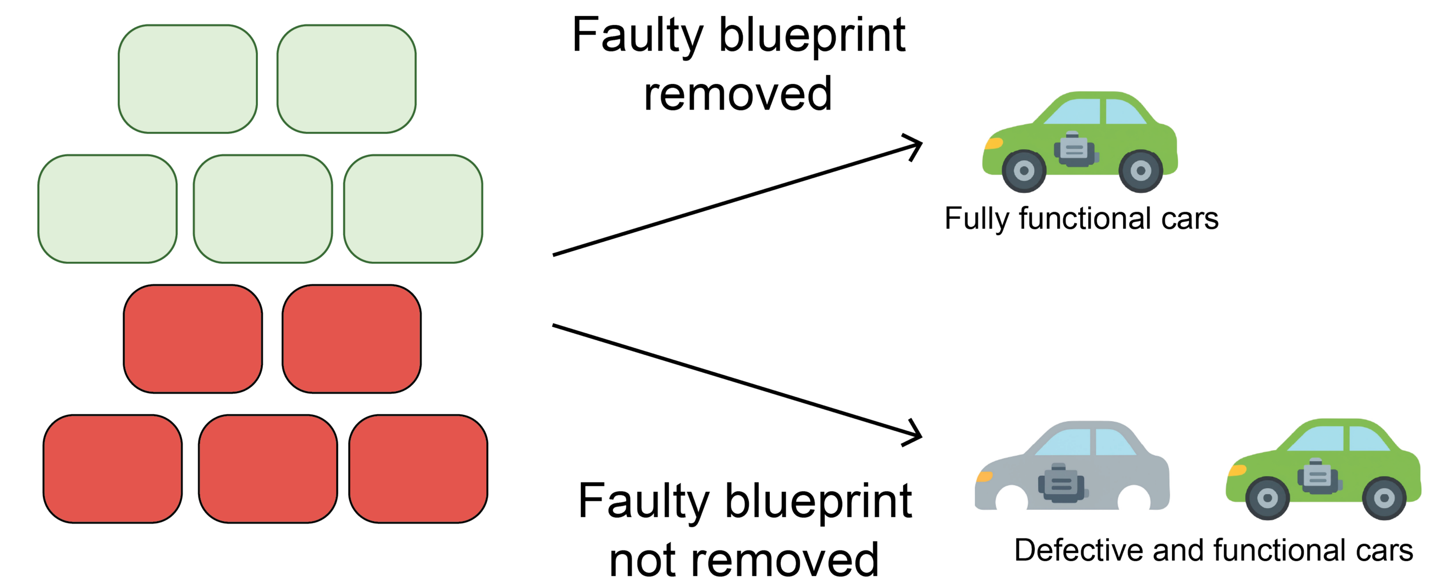


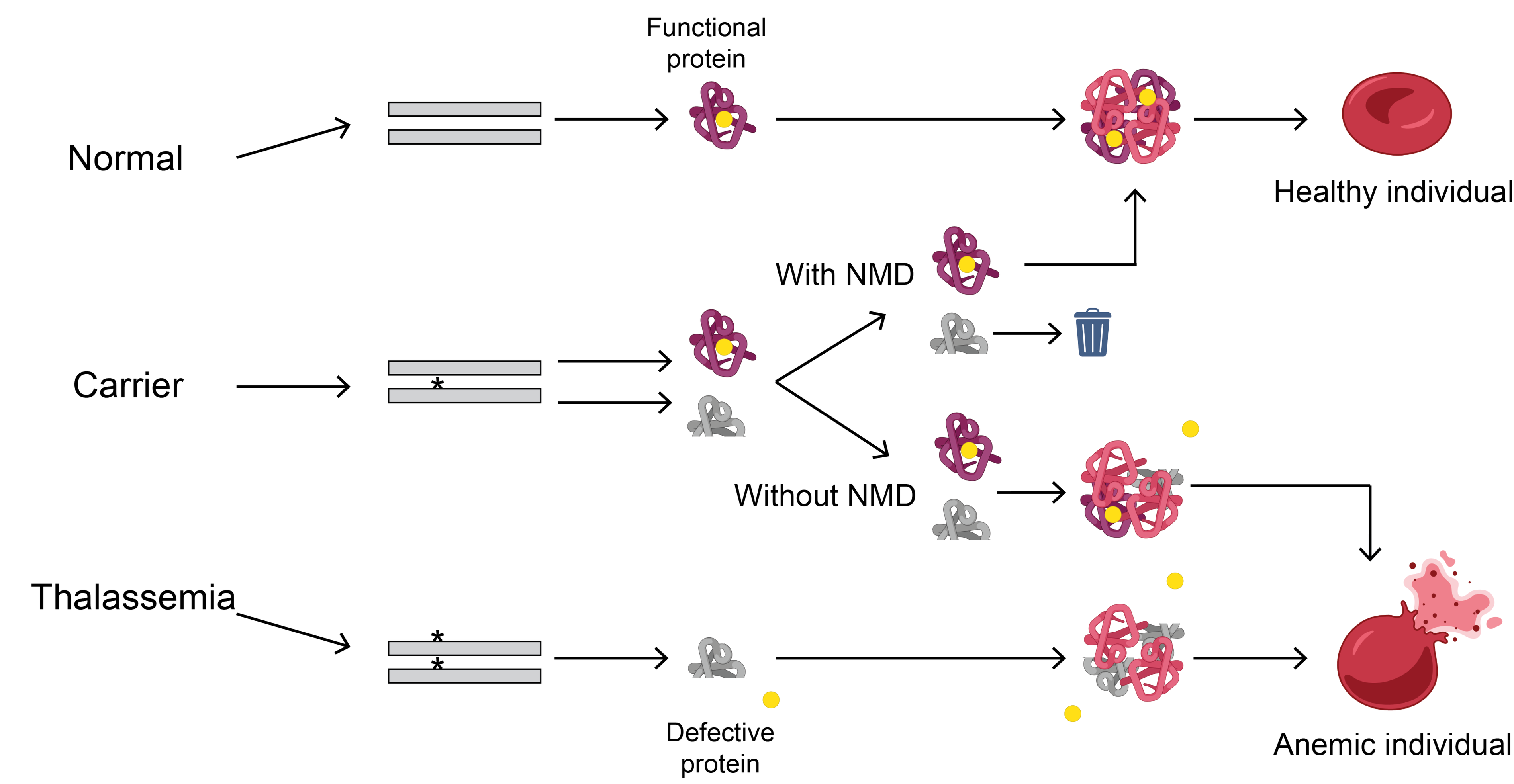
mRNA degradation



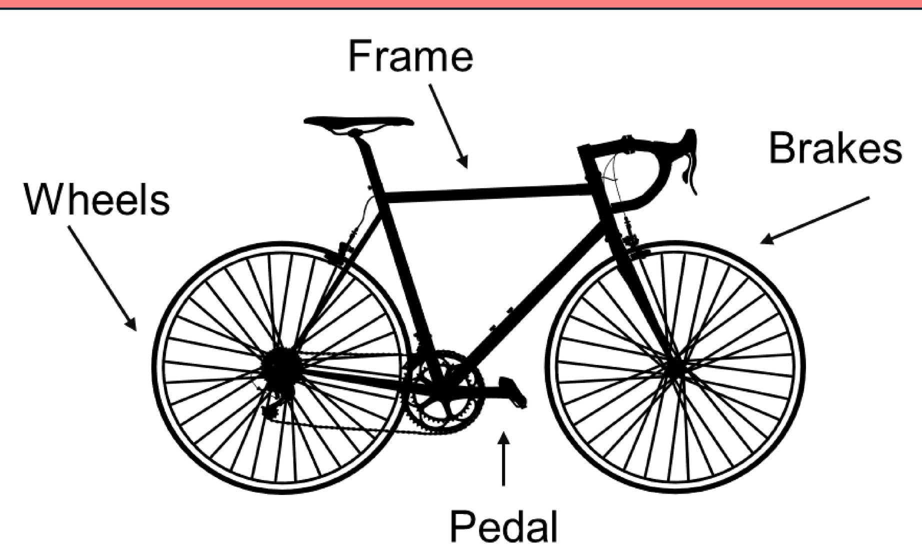
Limits formation of truncated proteins

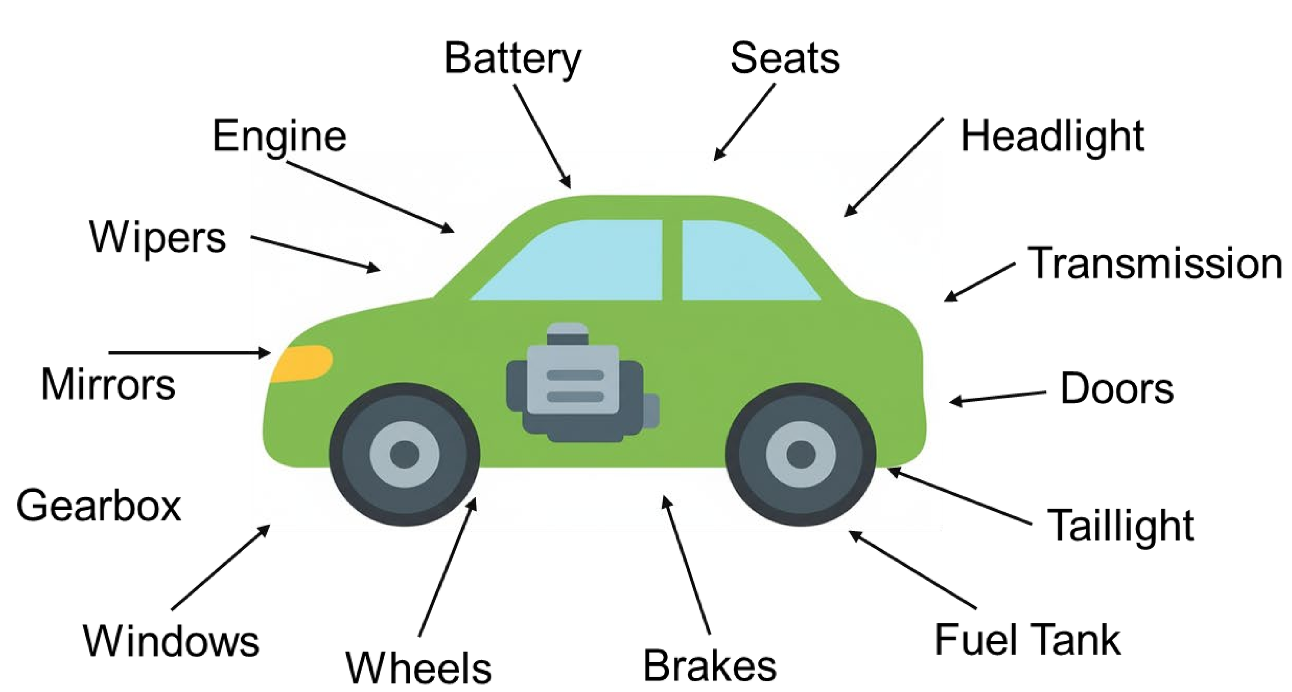
RNA surveillance by NMD can suppress disease-causing mutations



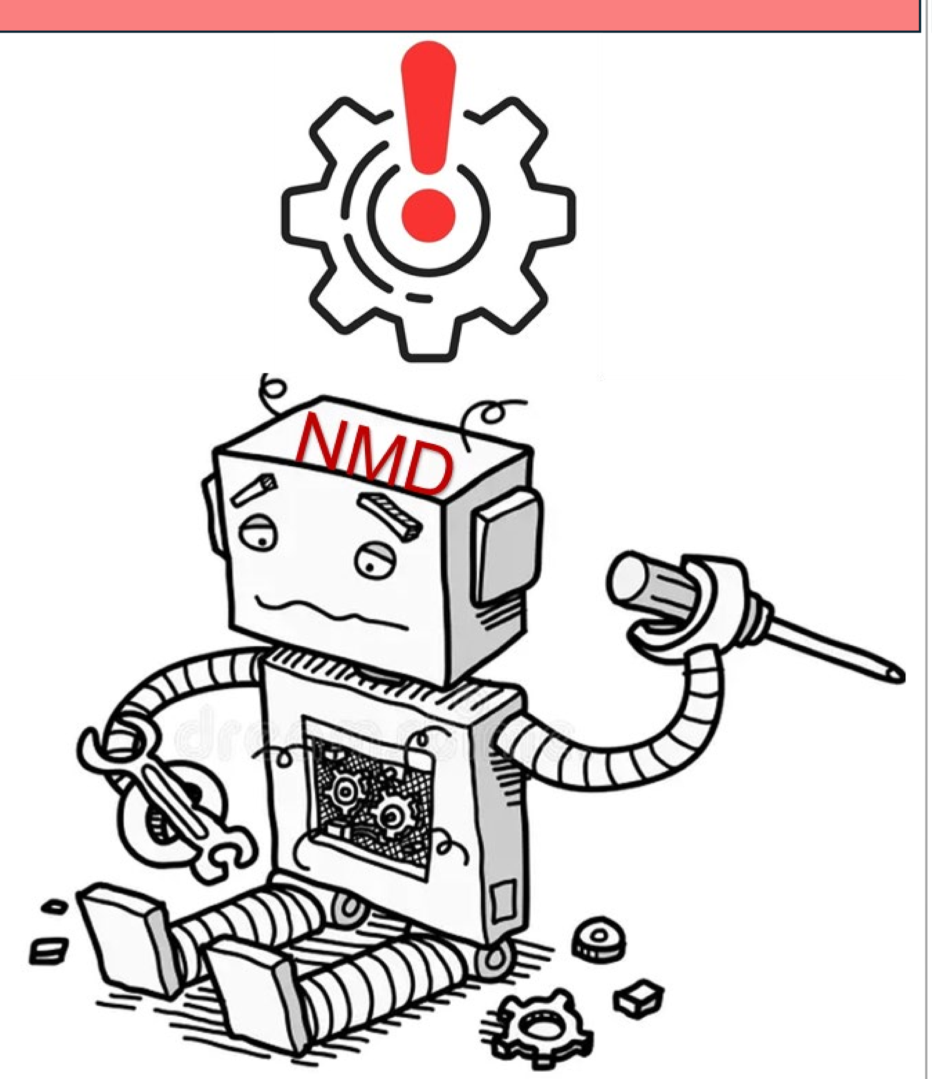


Complex systems are more prone to NMD failure





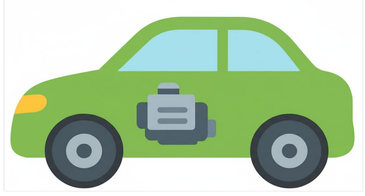
Quality control of a simple vs complex system



- **Microcephaly**
- **Autism Spectrum Disorders**
- **Intellectual Disability**
- **Faulty Immune System**
- **Tumor progression**
- **Embryonic Lethality**

Bypassing quality control can be useful in some disease contexts

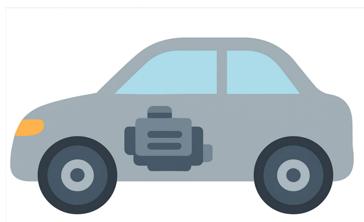
Normal blueprint (mRNA)
Attach wheels → install engine → paint the car green



perfectly functional car

Faulty blueprint (mRNA)
Attach wheels → install engine → **STOP**

inhibit NMD



car with slight imperfections (not painted) yet functional

normal NMD

no car produced

UPF3 is not essential for NMD: Functions as a modulator

Cystic Fibrosis | Duchenne Muscular Dystrophy | Spinal Muscular Atrophy

Faulty blueprint (mRNA)

↓

Partially functional protein

normal NMD	**inhibit NMD**
mRNA destroyed	**mRNA stabilized**
Limits protein production	**Allows production of useful protein**
Disease	**Treatment**

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