ASEF

SPEAKER SERIES

Predavanje bomo pričeli ob 19:03

asef.net

ASEF

AMERICAN SLOVENIAN EDUCATION FOUNDATION

- ASEF štipendijski program:
  - 10 tedenski raziskovalni obisk v tujini
  - ASEF tutorstvo
  - Delavnice, predavanja
  - Team building, izleti, ostali dogodki…
- ASEF Speaker Series

HARVARD UNIVERSITY

Stanford University

Berkeley UNIVERSITY OF CALIFORNIA

UNIVERSITY OF CAMBRIDGE

COLUMBIA UNIVERSITY IN THE CITY OF NEW YORK

PRINCETON UNIVERSITY

Retrotranspozoni: 'Trojanski konji' naših genov

prof. dr. Jernej Ule

Kemijski inštitut Ljubljana | Francis Crick Institute London | Dementia Research Institute at King's College London

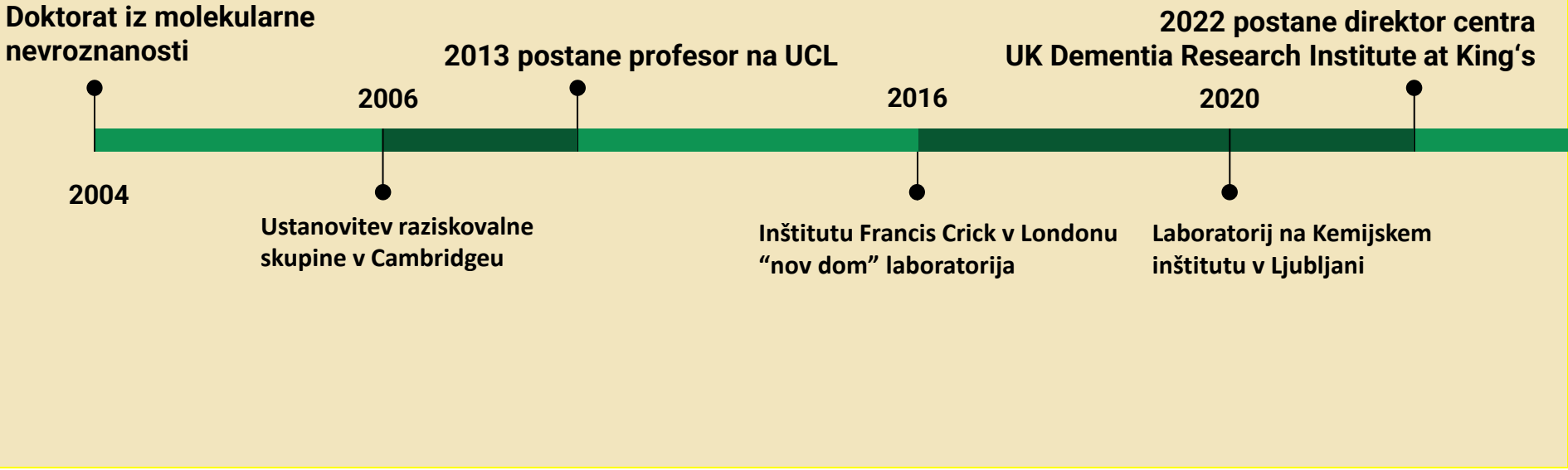
Torek, 14. marec ob 19:00 (CET)

Prešernova dvorana SAZU (Novi trg 4, 1000 LJ) | Zoom

ASEF

AMERICAN SLOVENIAN EDUCATION FOUNDATION

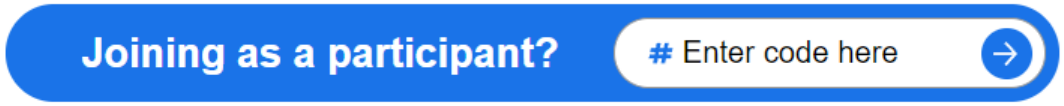
Prof. Dr. Jernej Ule

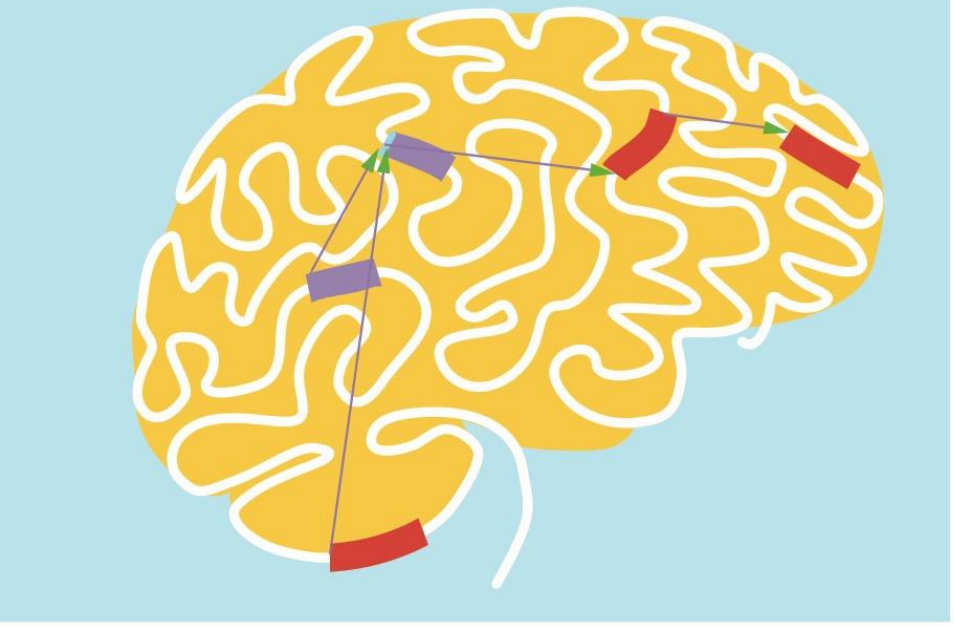


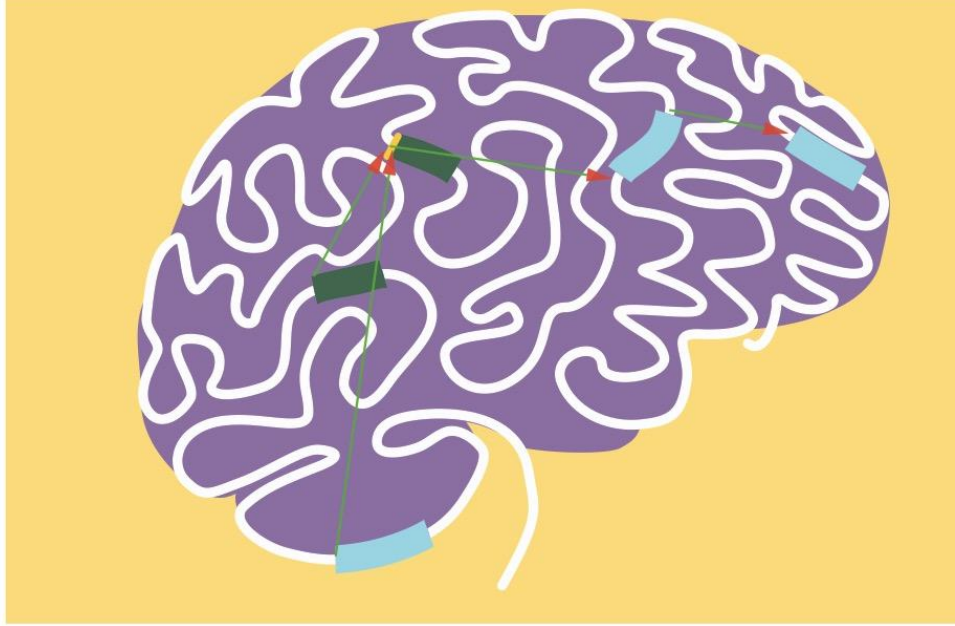
Vprašanja

- **KDAJ?** Na koncu predavanja

- **KAKO?** Vprašanja zastavite na www.sli.do s kodo ASEESpeakerSeries





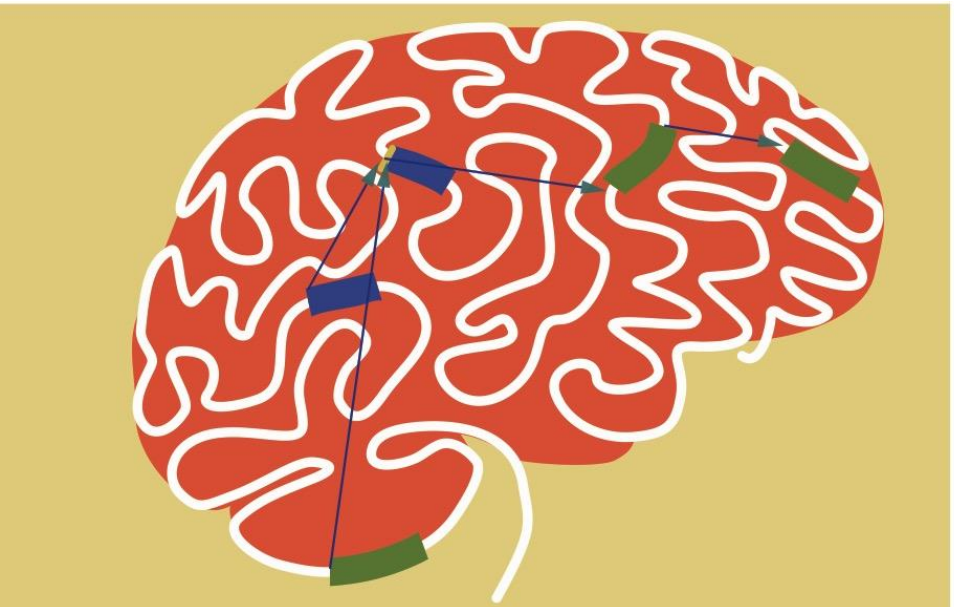


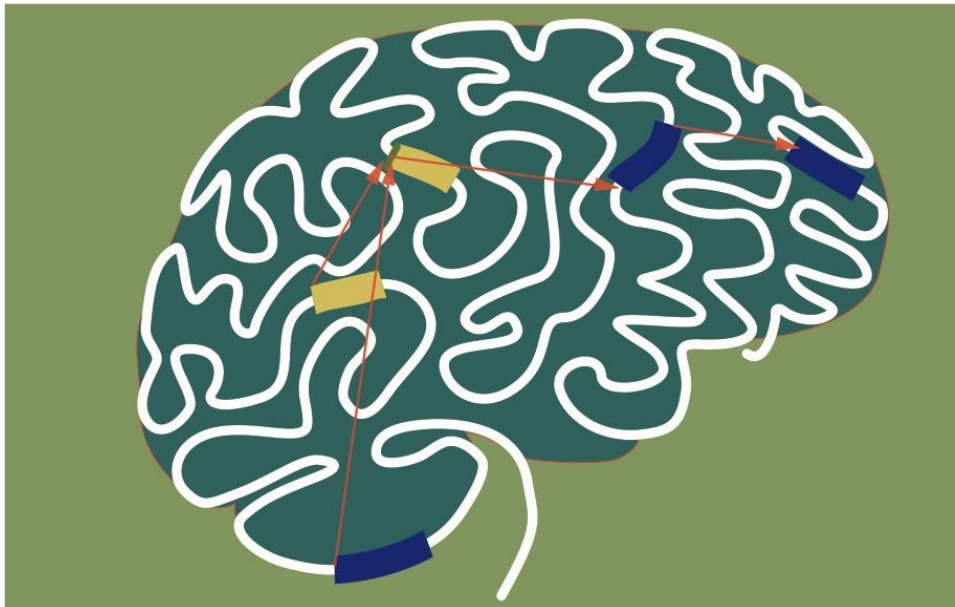
Retrotranspozoni: 'Trojanski konji' naših genov

Jernej Ule

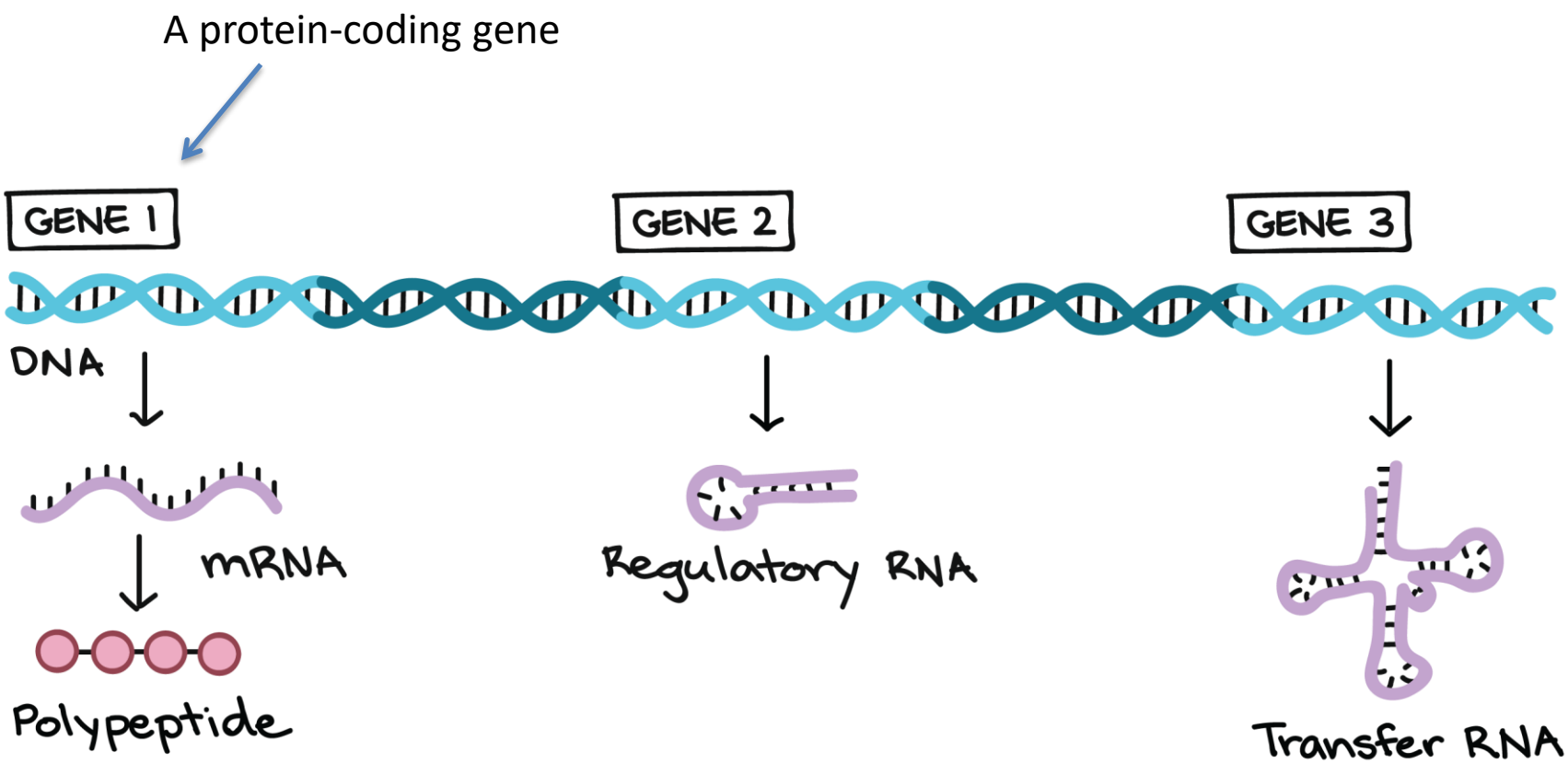
www.ulelab.info

Dementia Research Institute at King’s, The Francis Crick Institute, Slovenian Institute of Chemistry



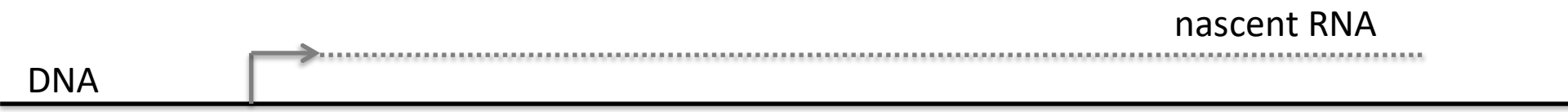


If DNA is a cookbook, RNAs are the recipes



https://www.khanacademy.org/science/high-school-biology/hs-molecular-genetics/hs-rna-and-protein-synthesis/a/intro-to-gene-expression-central-dogma

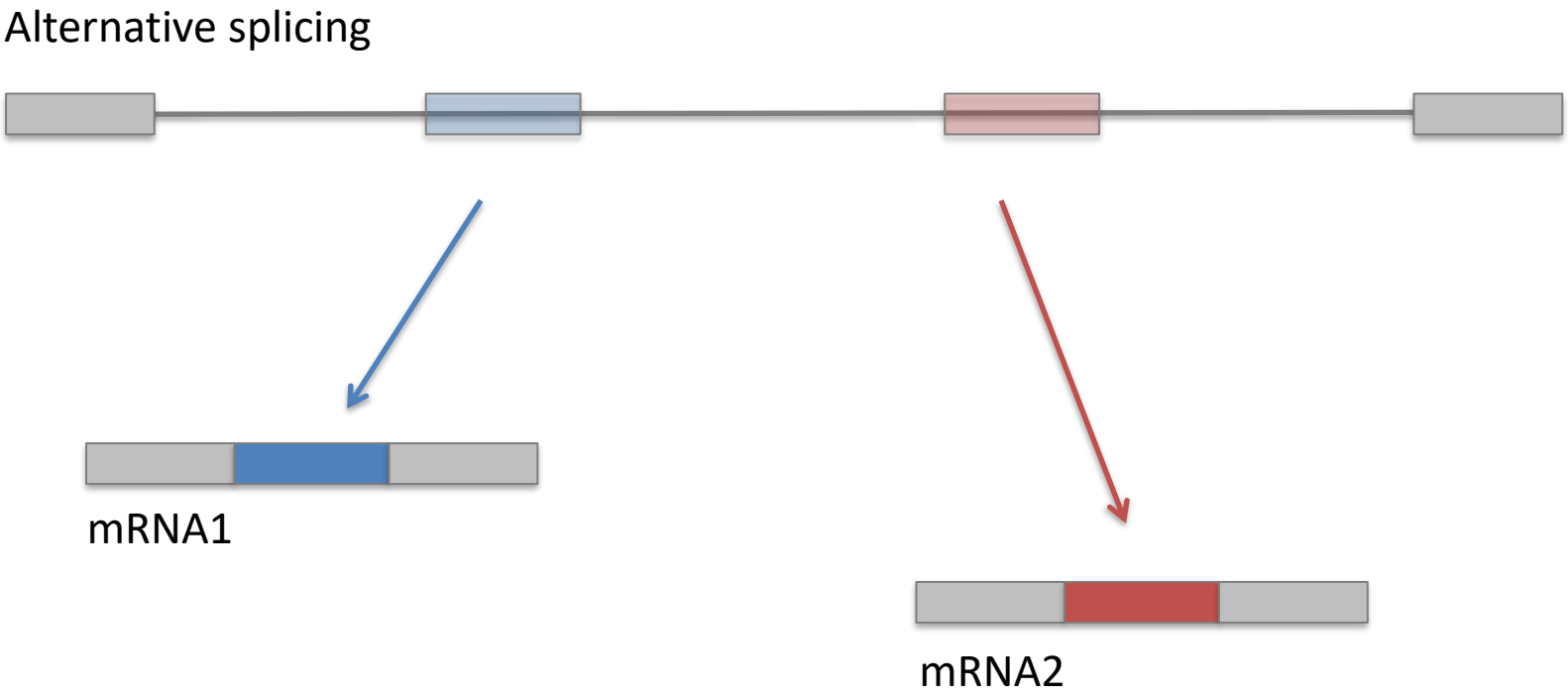
Each gene is first dutifully transcribed into a nascent RNA



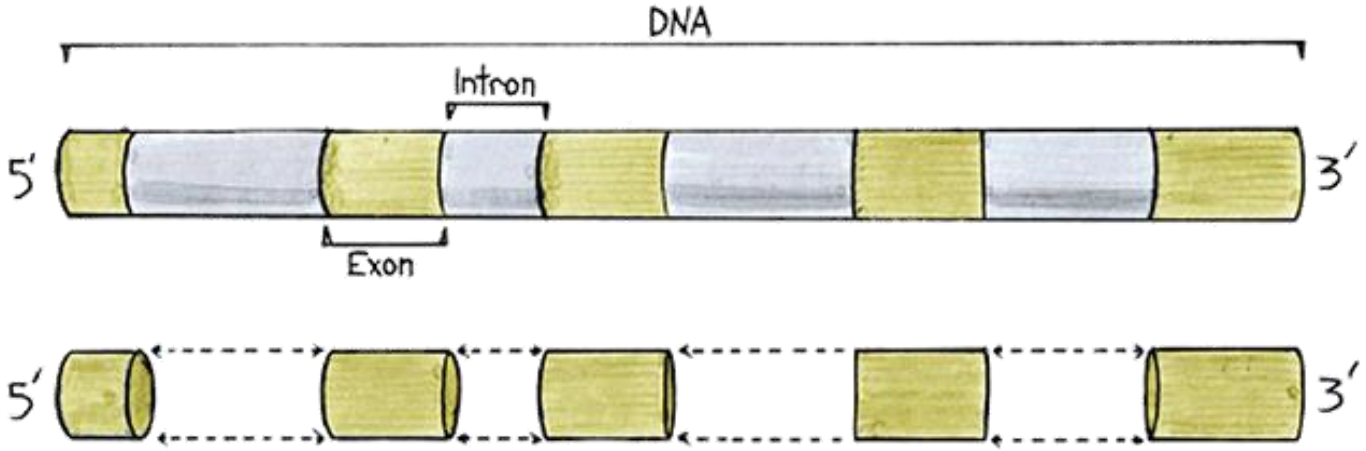
Each gene is first dutifully transcribed into a nascent RNA

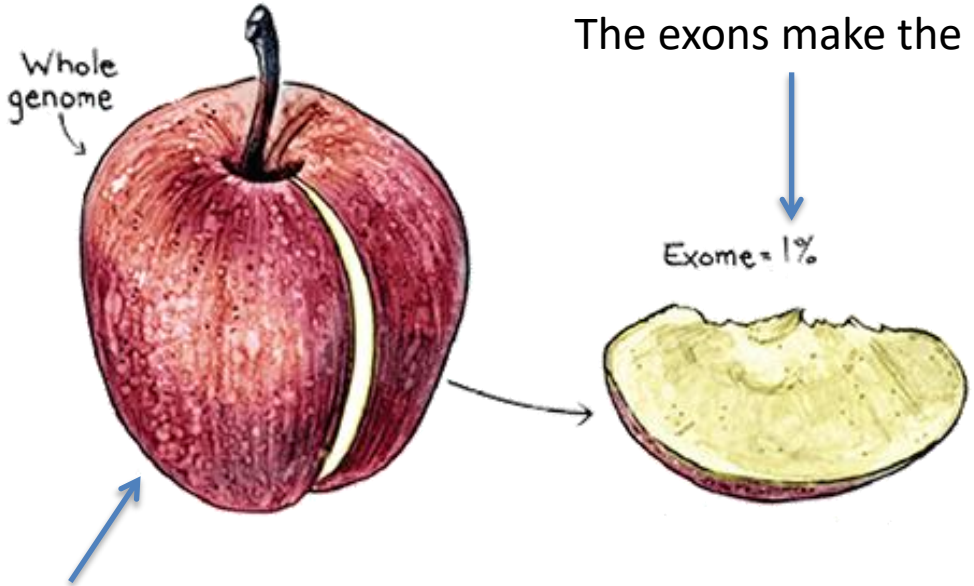
Only exons are used to make the final recipe, the 'mRNA'

Most genes can produce variant mRNA recipes



Only a tiny part of human genome makes the mRNA recipes!

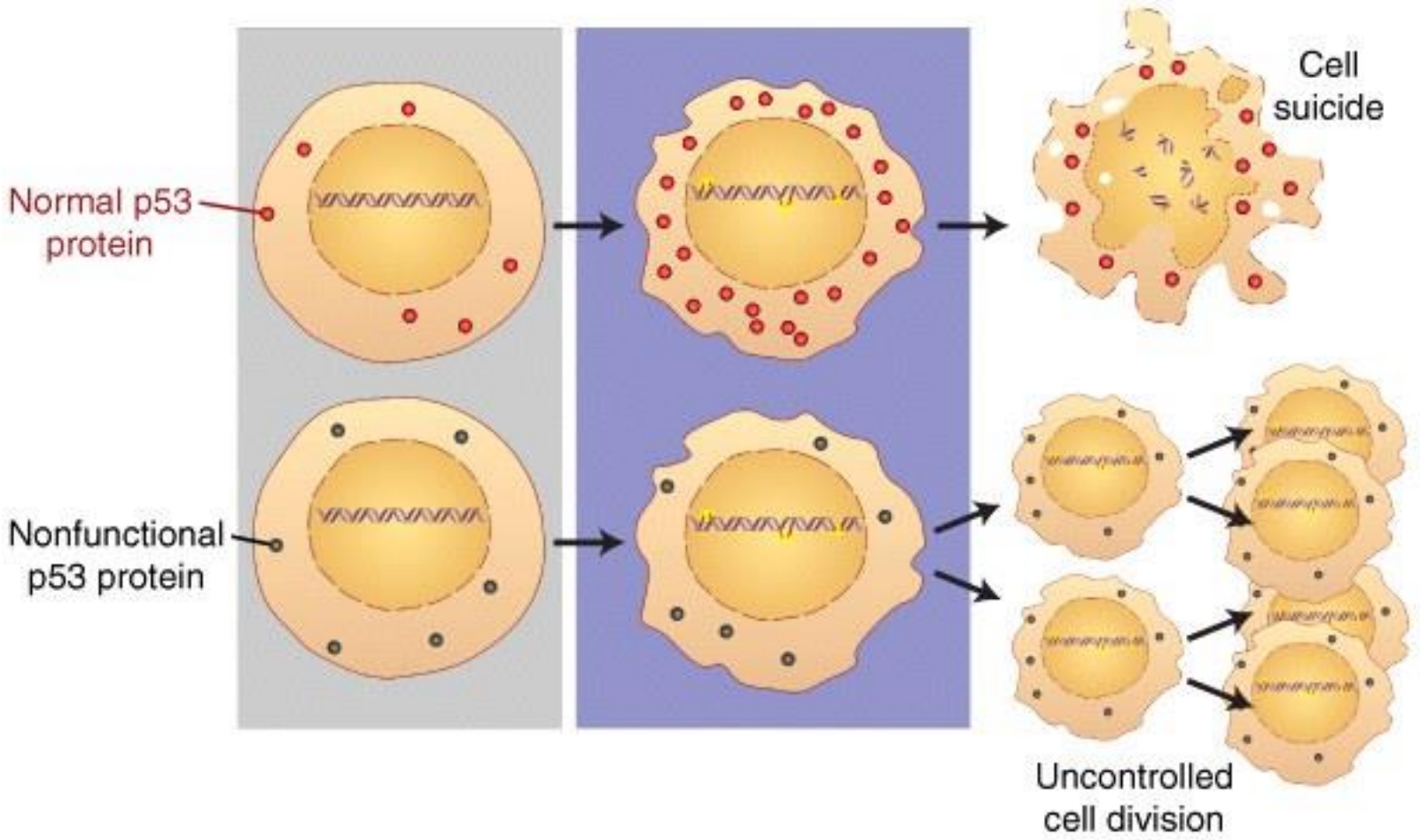




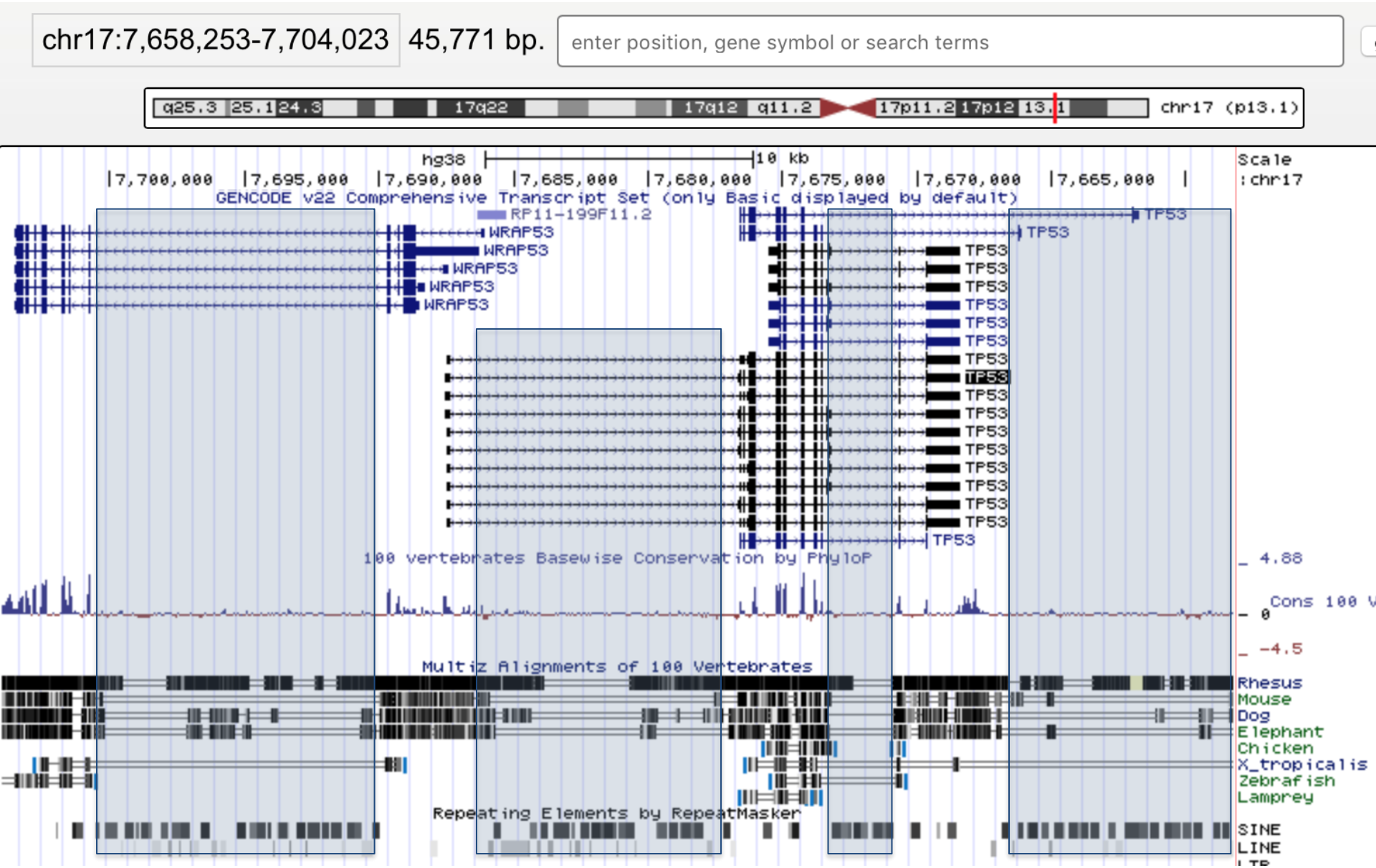
The exons make the mRNA recipes.

This contains instructions for when and how the recipes are made.

P53: a protein protecting us from cancer

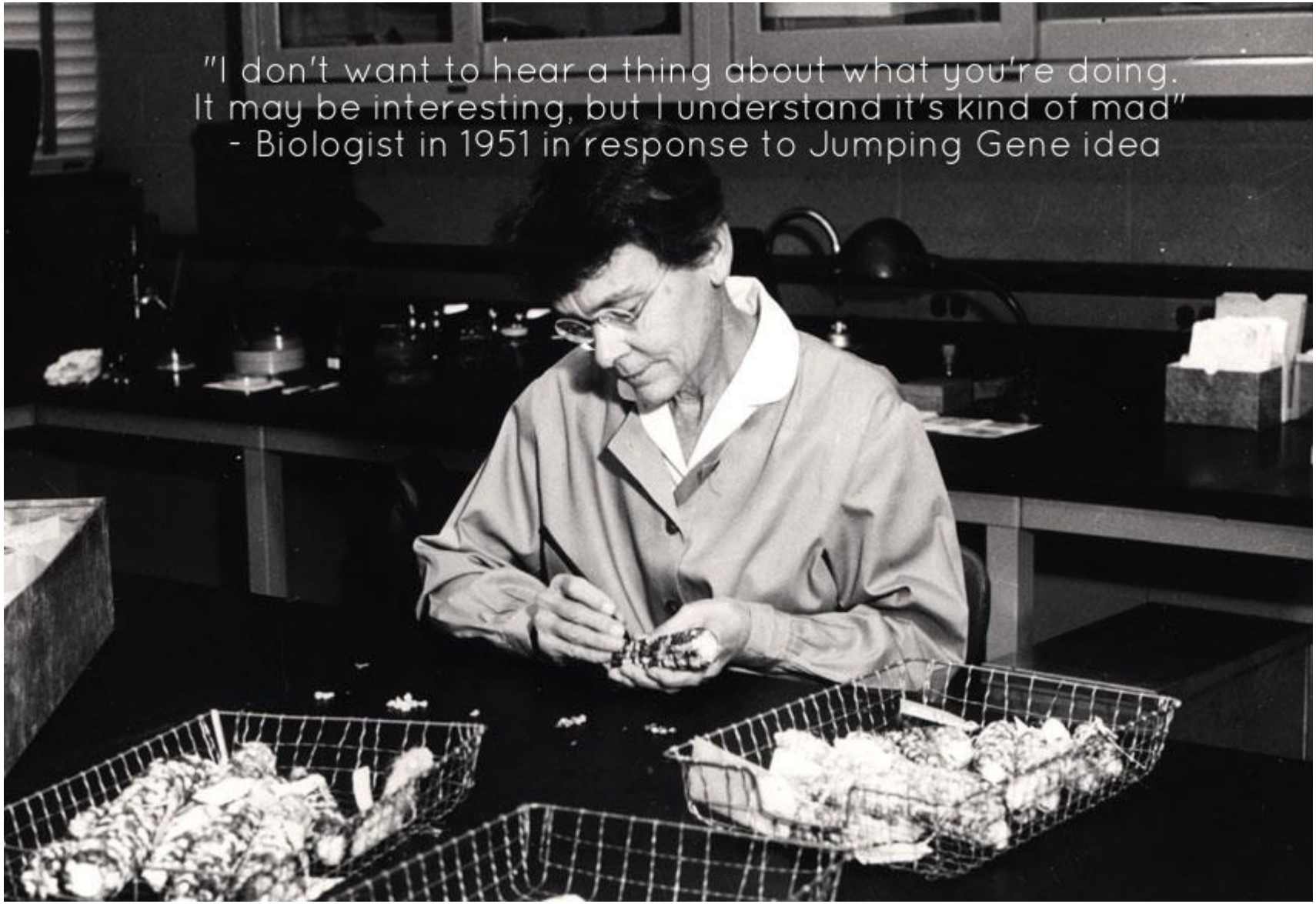


P53 gene in the human genome

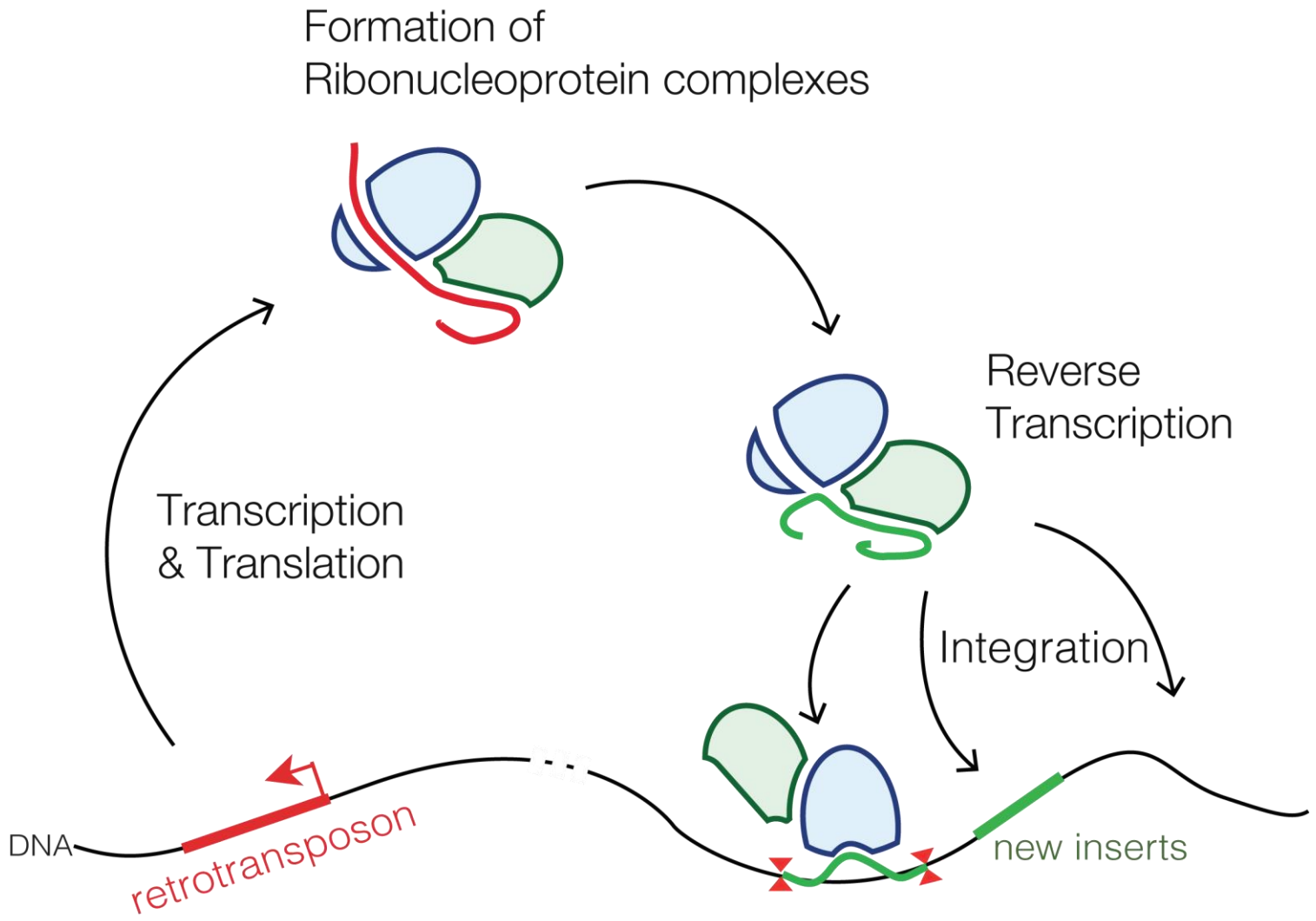


Barbara McClintock

Barbara McClintock

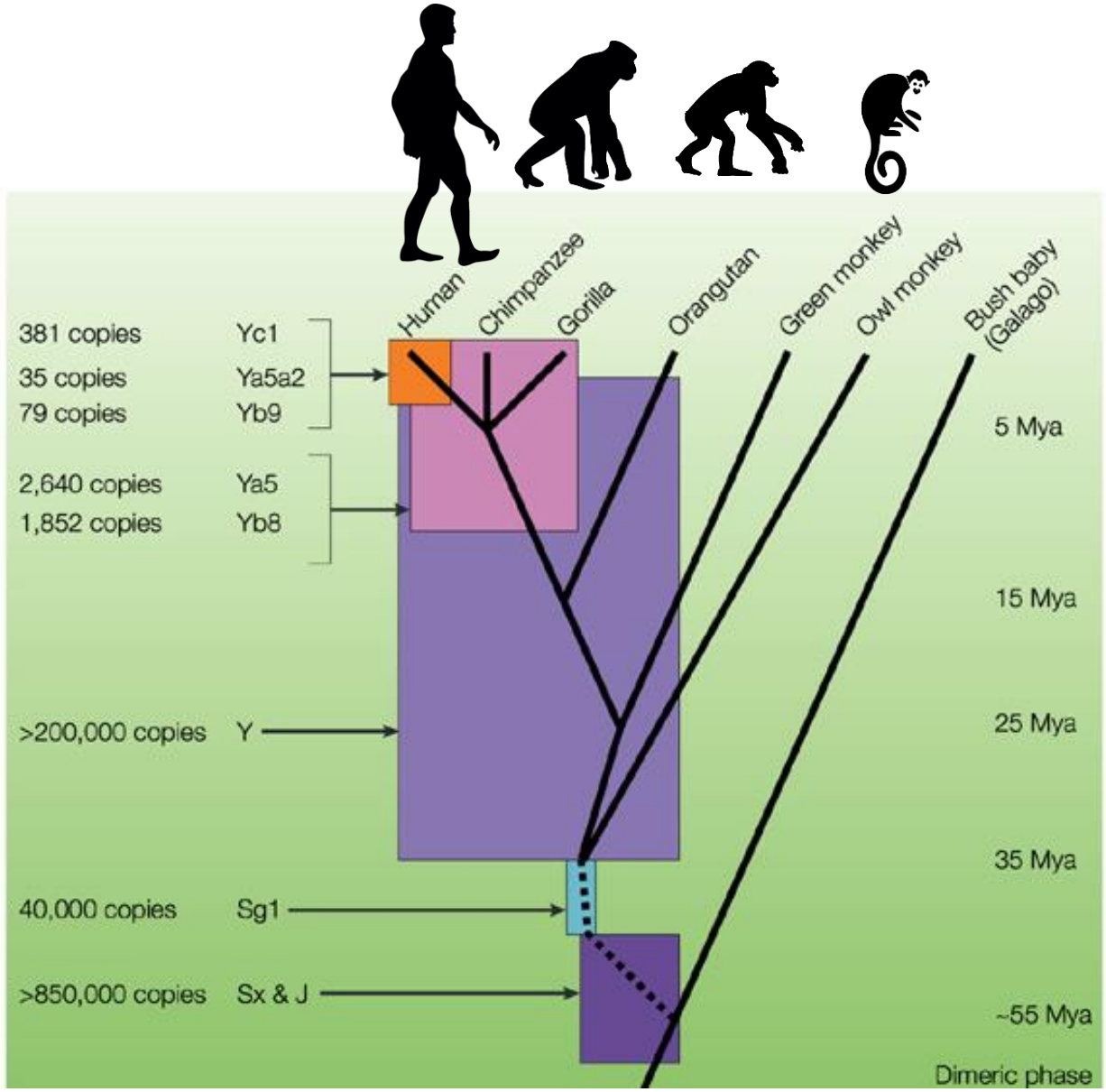


Retrotransposons are a common source of repetitive sequences



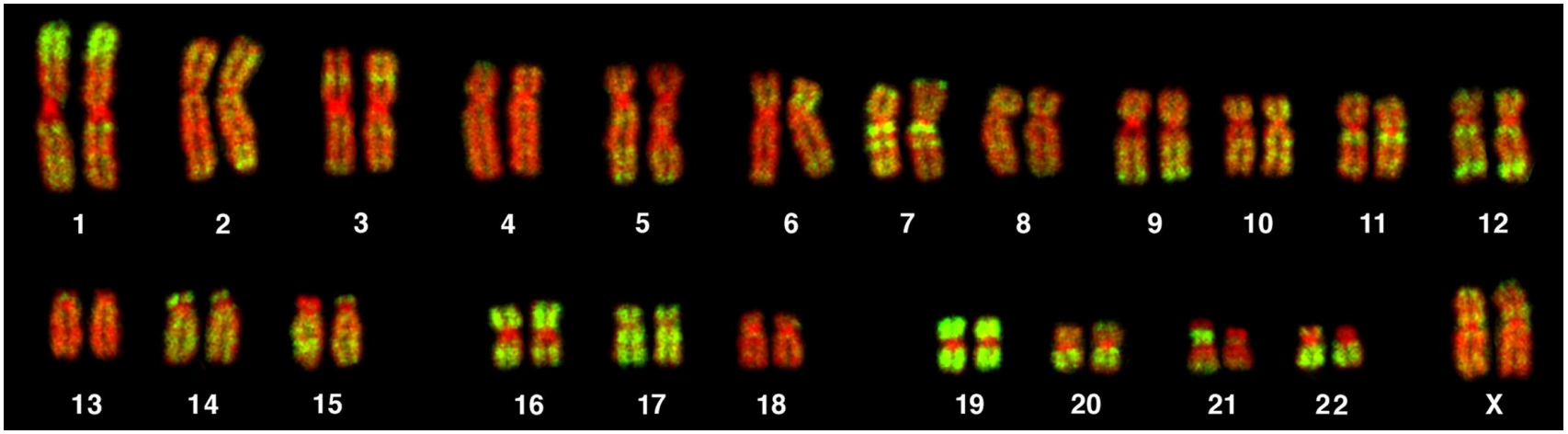
Reece et al, Campbell Biology (10th Edition), 2013

Alus are primate-specific retrotransposons



Batzer et al, Nat Rev Gen 2002

Alu elements in the human genome

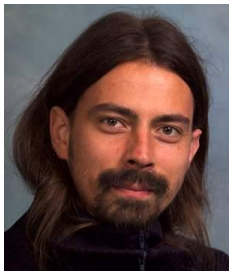


Alu elements are stained in green

Bolzer et al, PLOS Biology, 2005

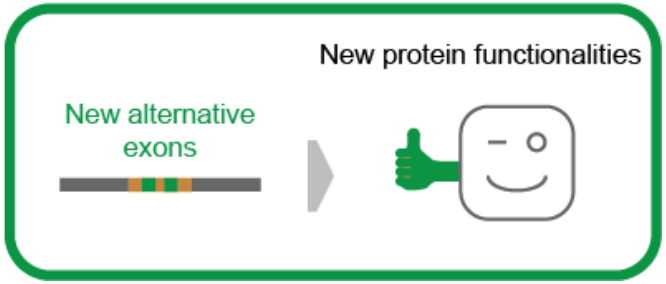
Many thousands of Alus contain sequences that can make exons

Kathi Zarnack
Frankfurt U.



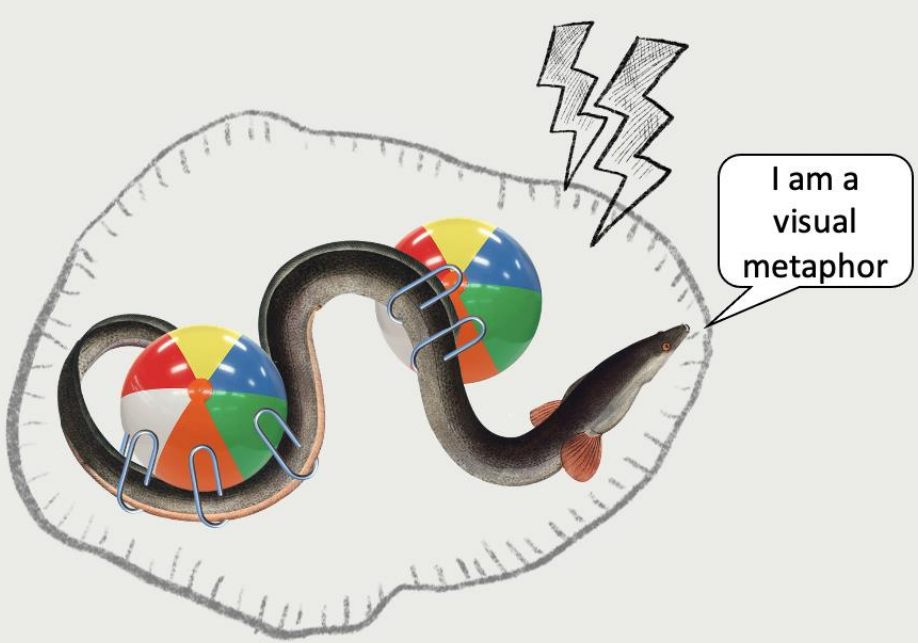
Julian König,
IMB Mainz

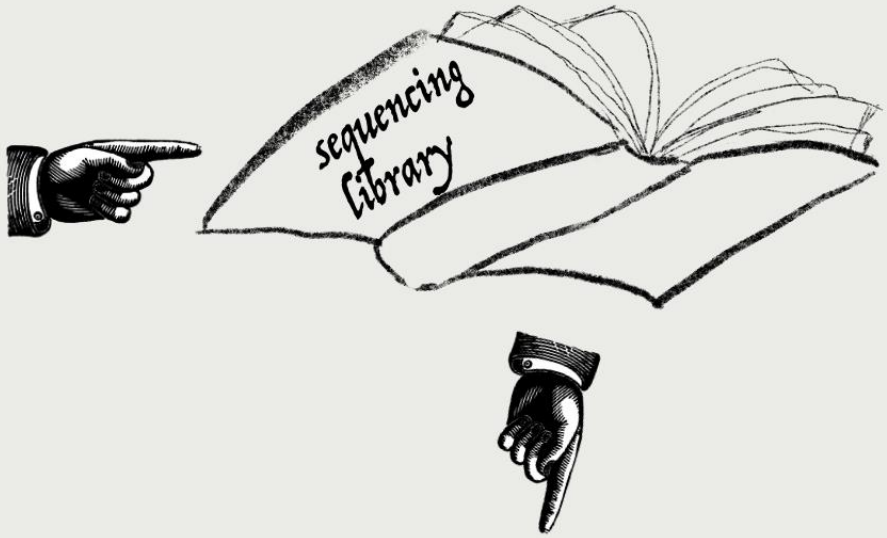
Nick Luscombe
Crick Institute



Zarnack et al, Cell, 2015

We use crosslinking and immunoprecipitation (CLIP) to identify protein-RNA interactions



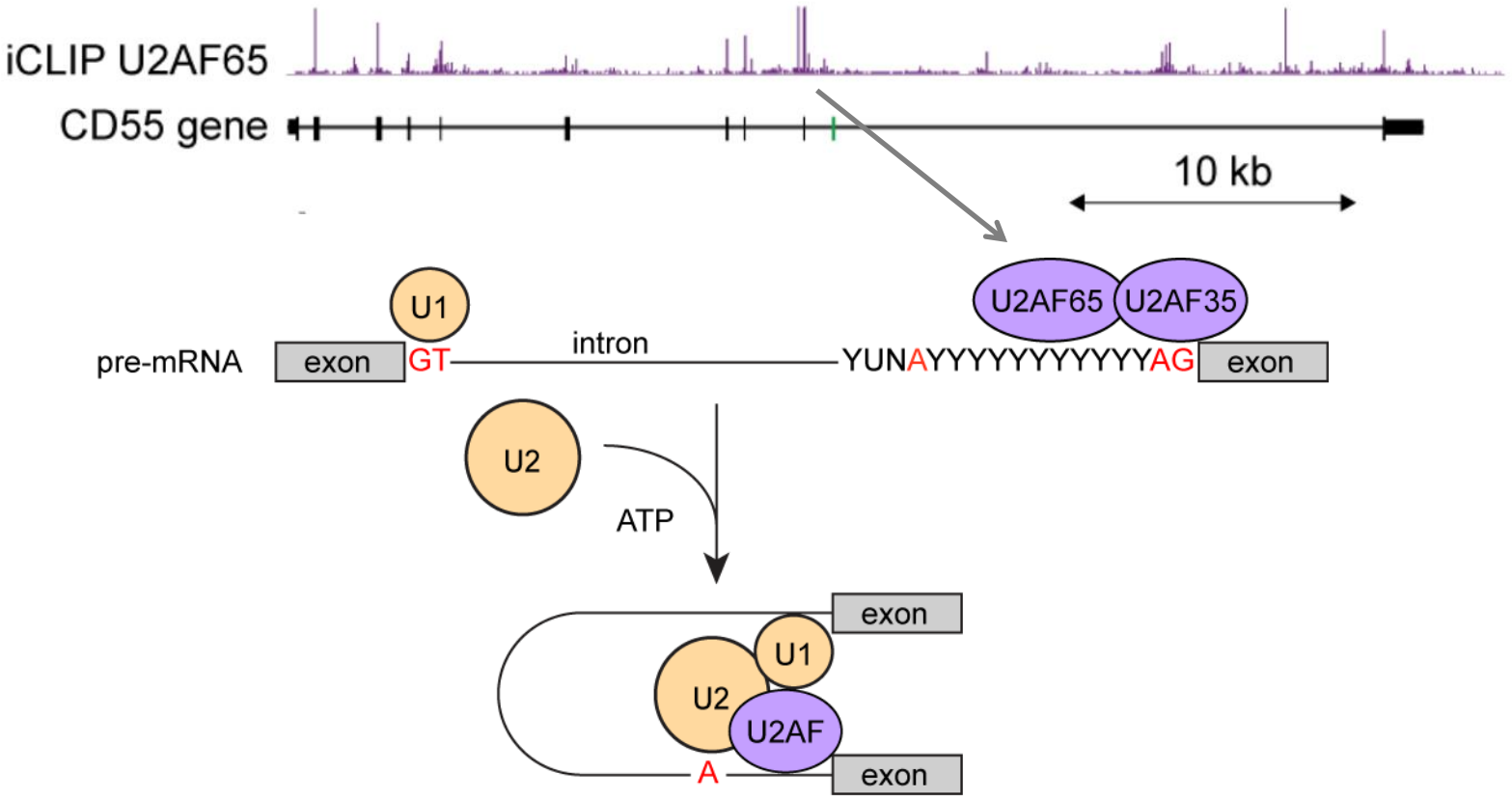



```
@HWI-EAS350_0863:3:1:4782:1006#0/1_341:rbc:NGCCA
CCTGGGTTCGAATCCCAGCGGTGCCTCAACCGAGCGAA
+
M__b__b_b_b_____________YYYYYYYYYY__
```

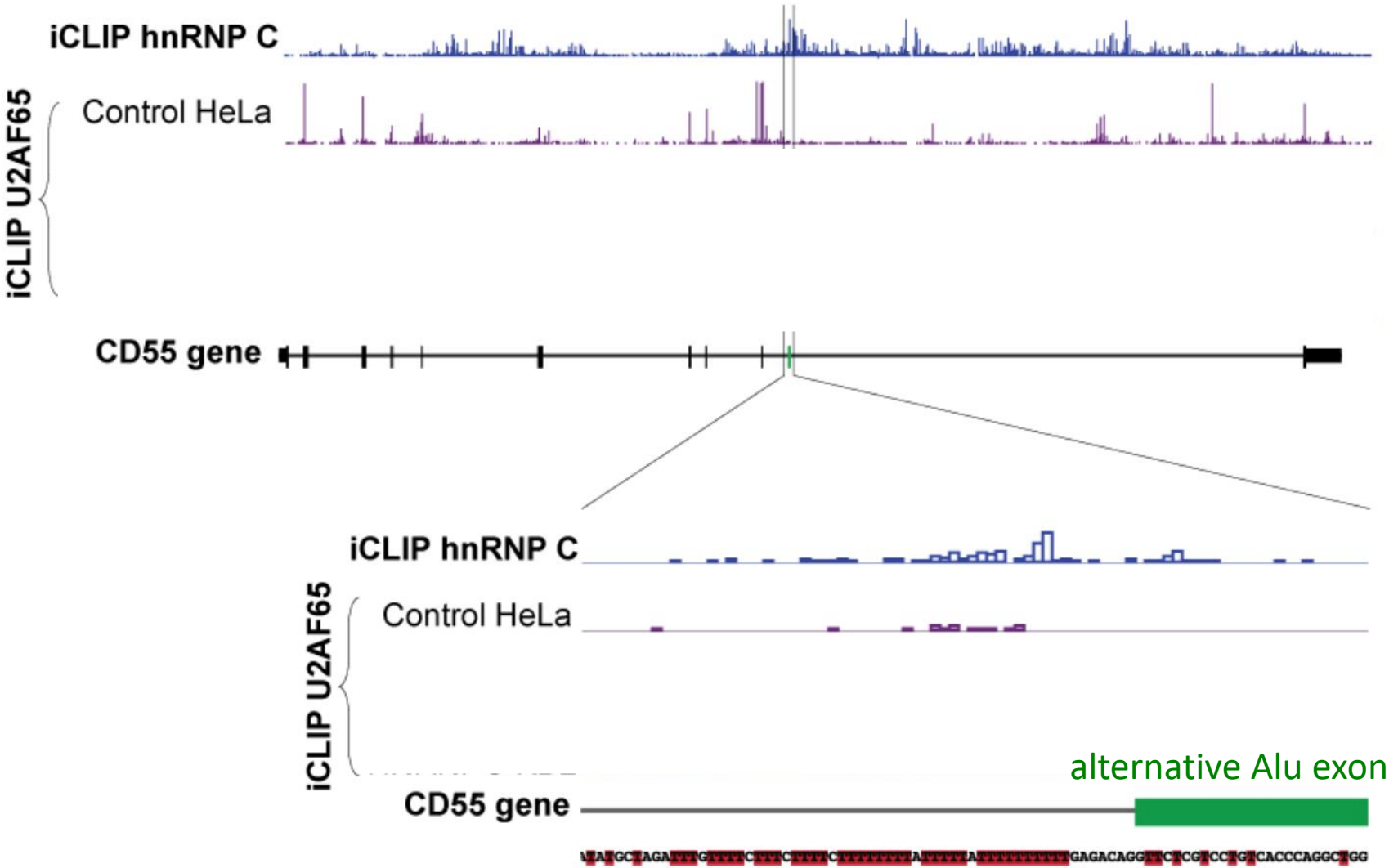
Lee et al, ‘An improved iCLIP protocol’, bioRxiv 2021

Also reports a protocol for input iCLIP control: Input-SP3

hnRNP C displaces U2AF65 from introns



hnRNP C displaces U2AF65 from introns

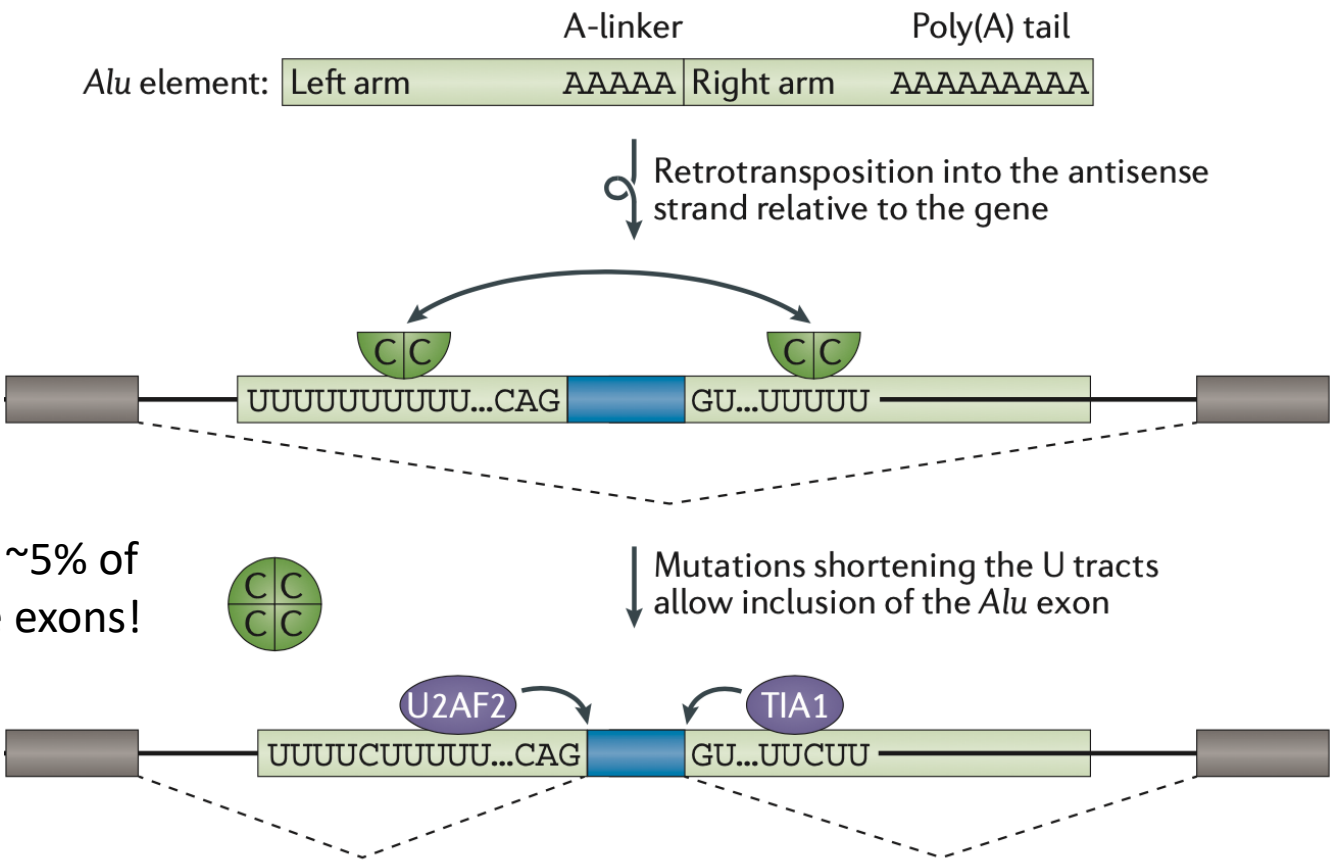


Zarnack et al., Cell 2013

Alu elements are a source of new exons in primate

*Alu*s resemble exons when in antisense orientation in introns

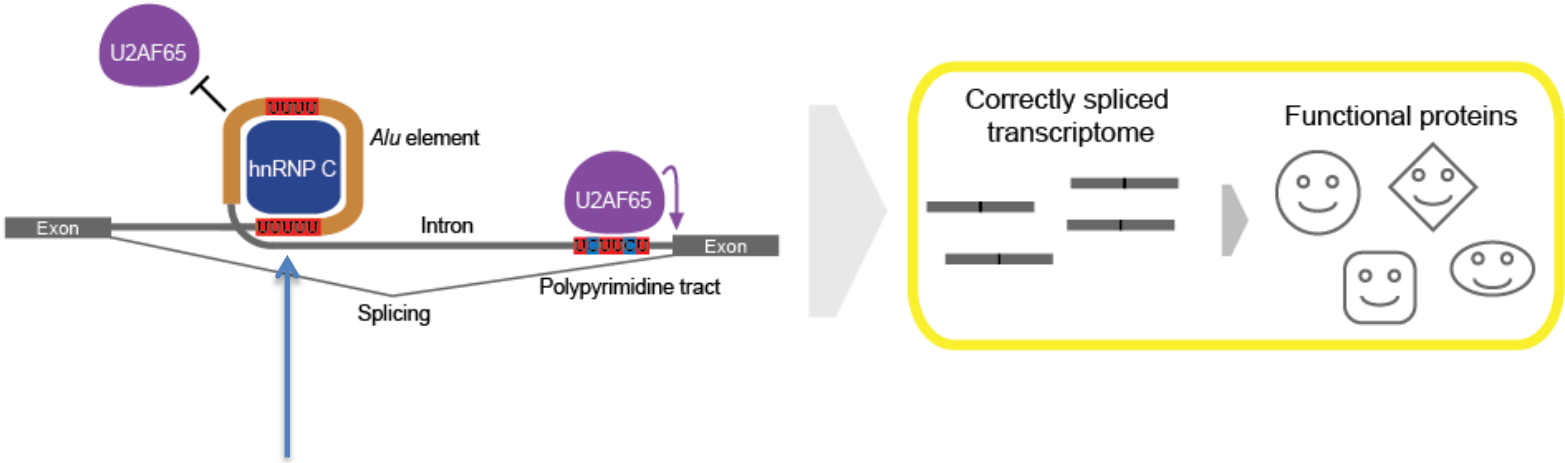
- cryptic 5’ and 3’ splice sites
- poly-U tracts



Alus contribute to ~5% of human alternative exons!

Sibley et al, Nat Rev Gen, 2016

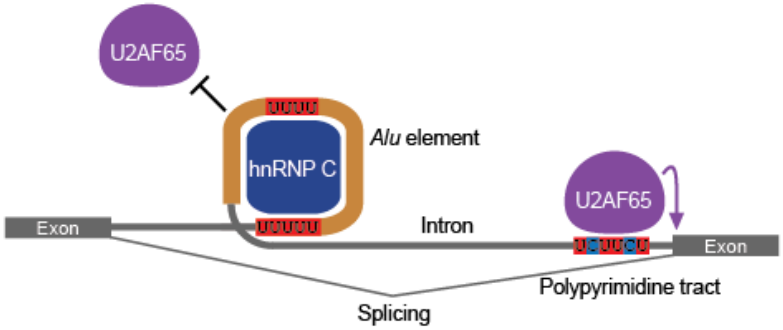
We discovered a protein that masks the Alu-exons

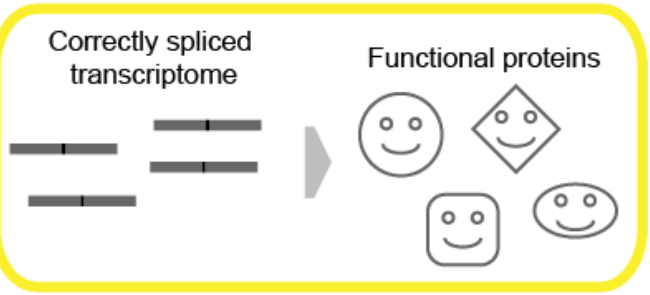


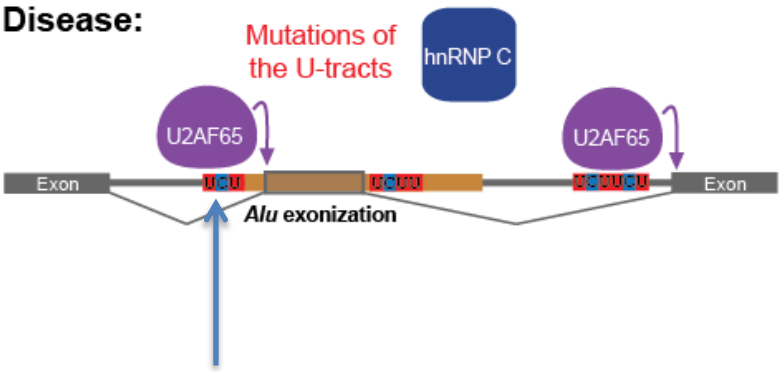
The ‘mask’ is attached to the U-tracts (such as UUUUUUUU) inside Alus

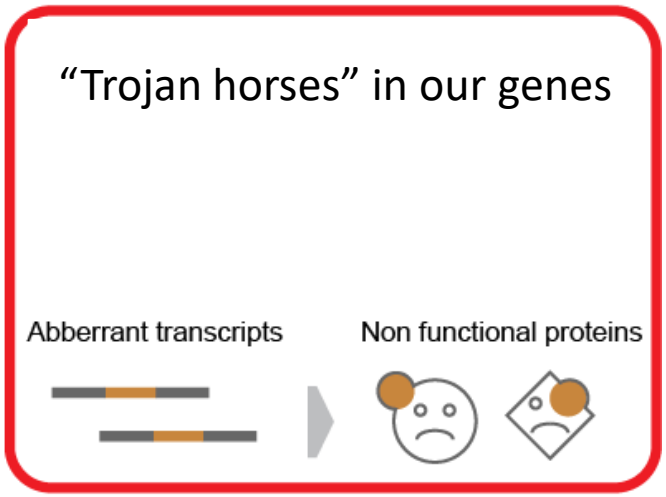
Zarnack et al, Cell, 2015

Mutations can shorten U-tracts to unmask the Alu-exons



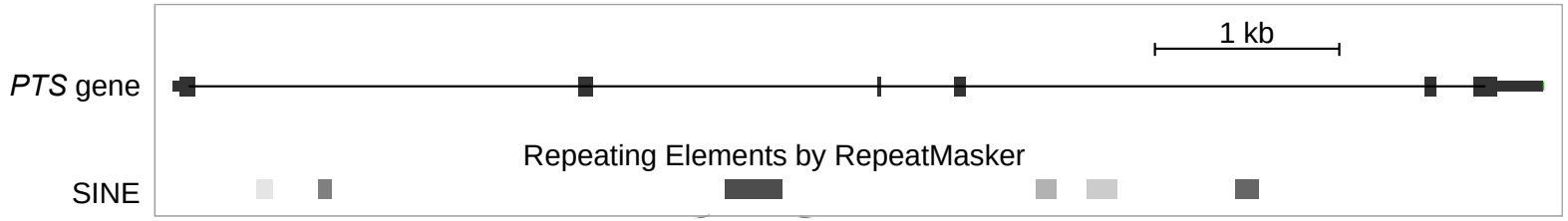






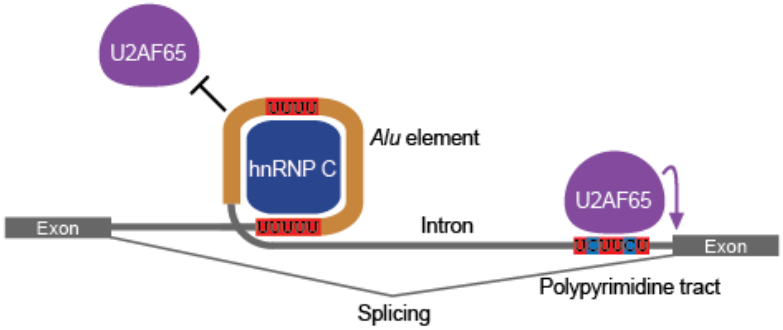
Mutations in U-tract unmask the Alu-exon, and thereby change the mRNA recipe

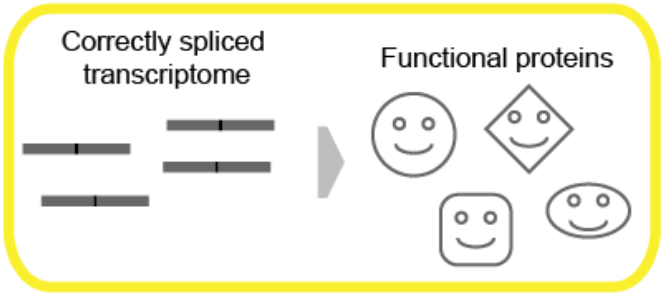
A mutation in the hnRNP C binding site leads to neurologic disease



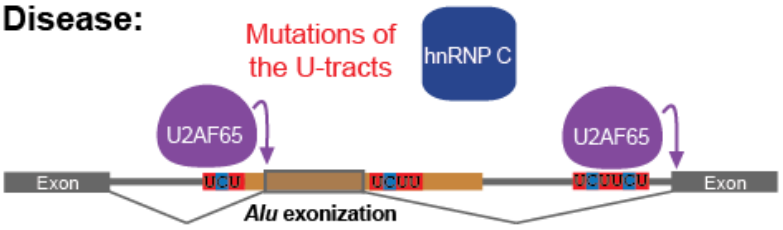
Zarnack et al, Cell, 2013

With additional mutations, beneficial Alu-exons can evolve

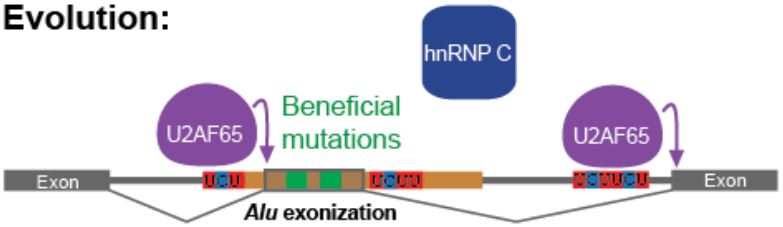


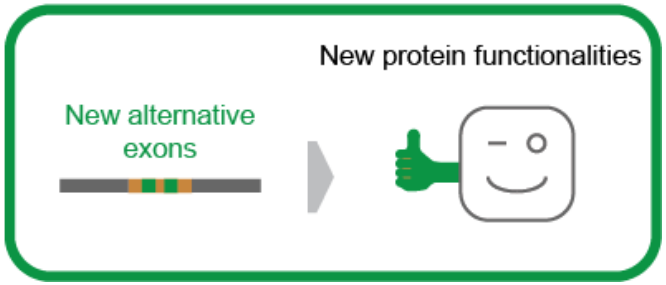


Disease:

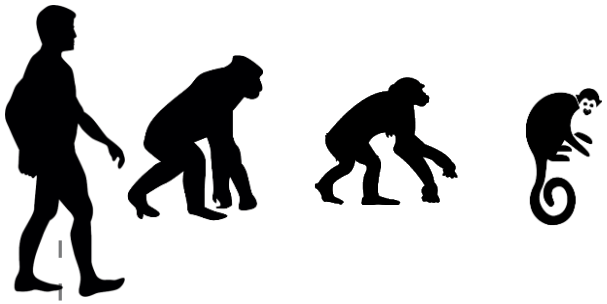


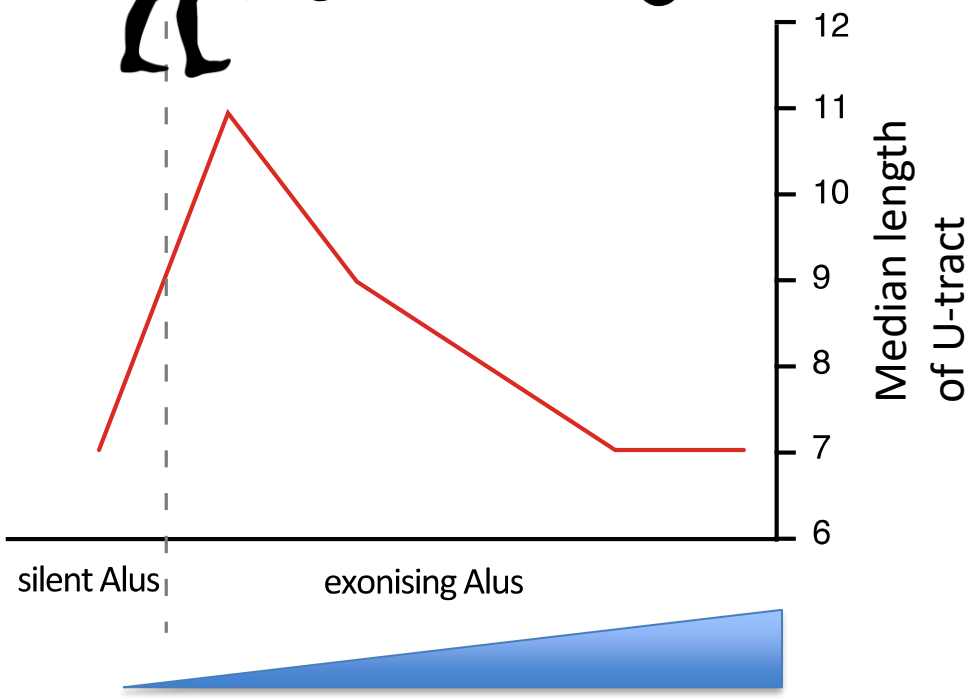
Evolution:





Alu U-tracts are like a tunable dimmer controls for graduate evolution.





Contribution towards the RNA recipes

Jan Attig

Nejc Haberman

Aarti Singh

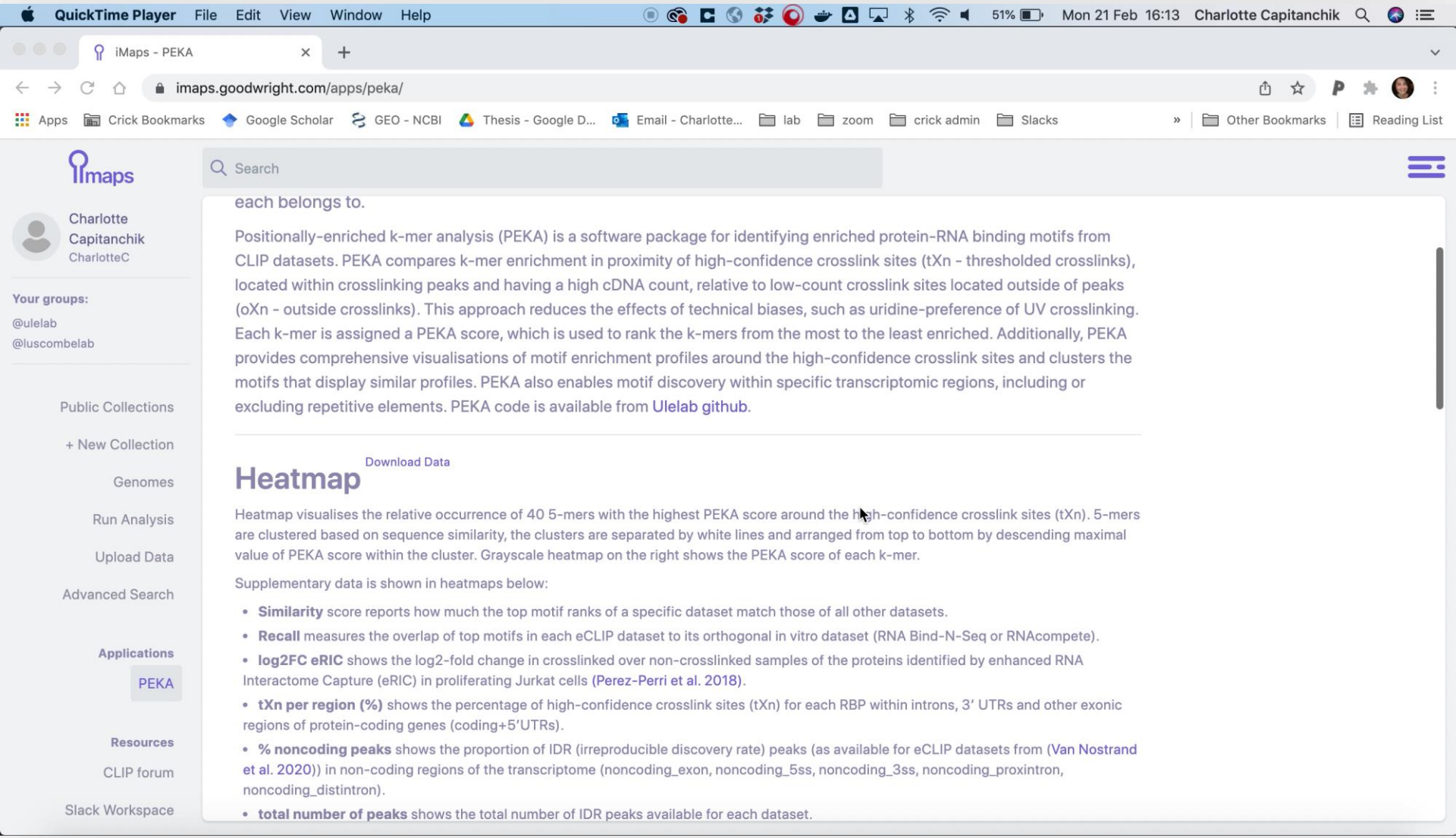
Attig et al, eLife, 2016

Klara Kuret

https://github.com/ulelab/peka

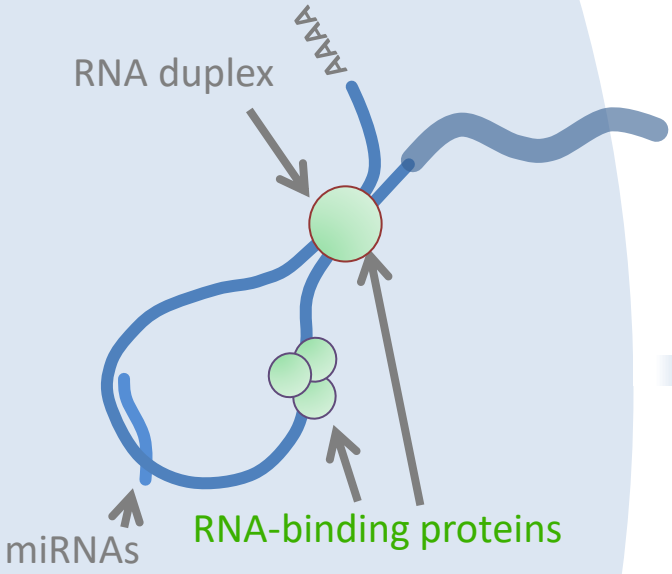
“Positional motif analysis reveals the extent of specificity of protein-RNA interactions observed by CLIP” Kuret et al., Genome biology, 2022

https://imaps.goodwright.com/apps/peka/



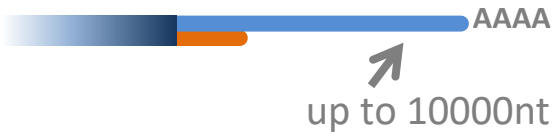
Kuret et al, Genome biology, 2022

Protein-RNA complexes

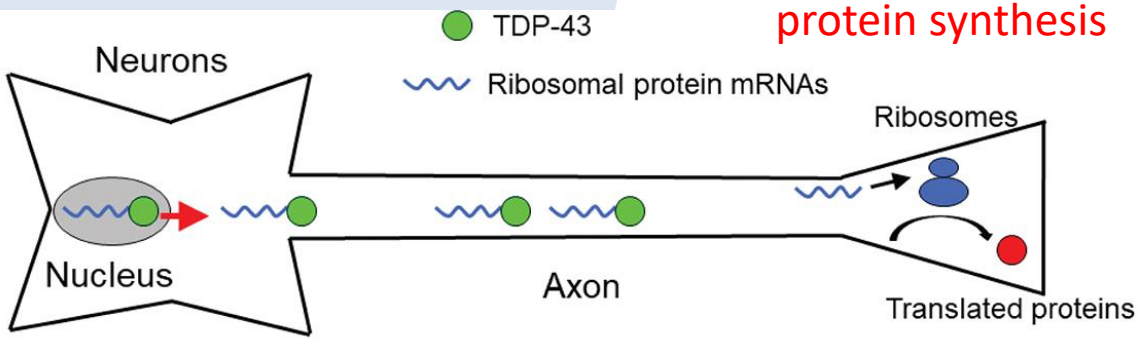


Neuronal regulatory functions

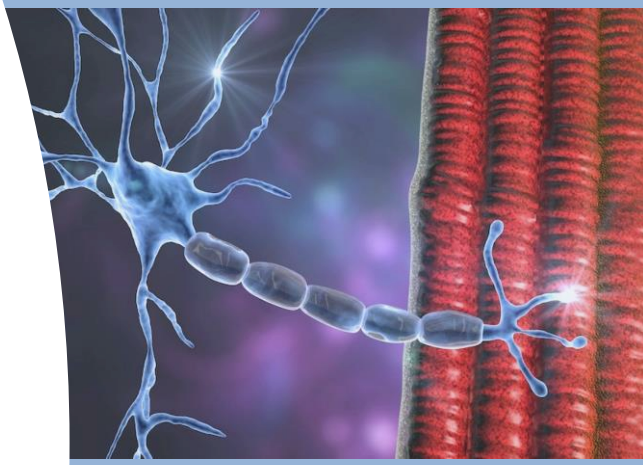
Long 3'UTRs of neuronal mRNAs



mRNAs are transported to allow localised protein synthesis



Amyotrophic lateral sclerosis (ALS)

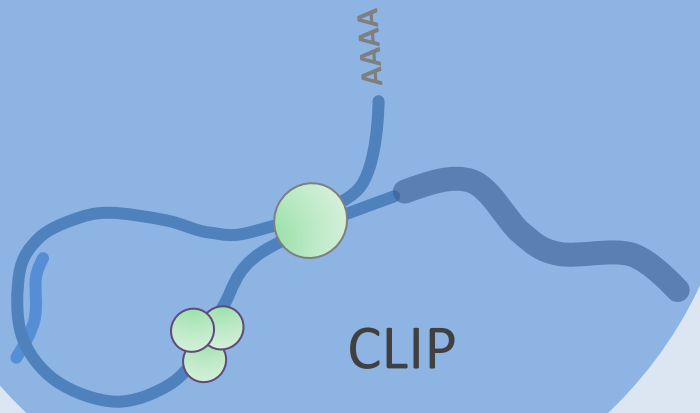


No cure available
Lifetime risk ±1/400 in UK

Mutations in >10 genes encoding RNA-binding proteins can cause ALS

Measure interactions

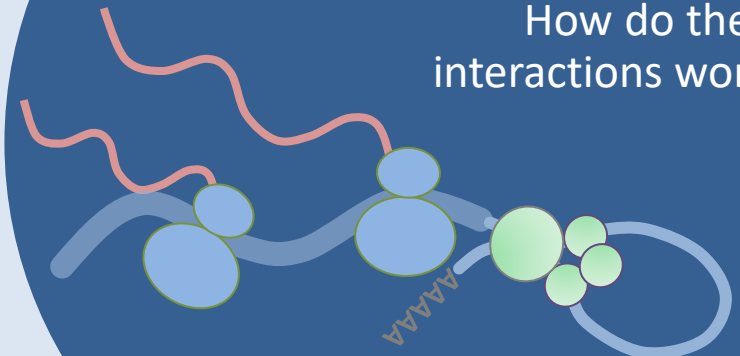
Which interactions drive the assembly of protein-RNA complexes?



CLIP

Integrate layers of data

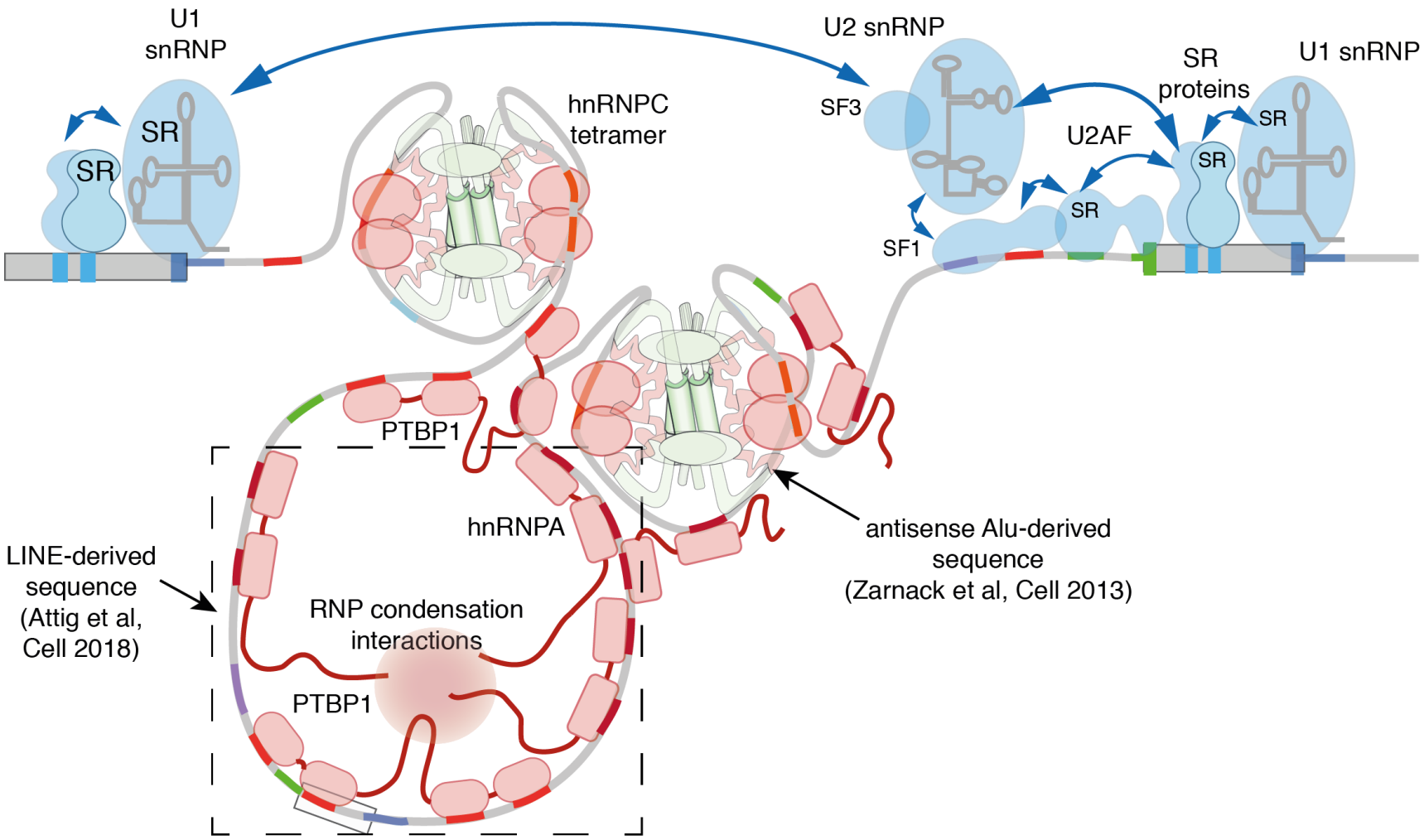
How do these interactions work?



https://flow.bio/

Interpret mutations

How do mutations disrupt protein-RNA complex assembly?



Attig et al, Cell, 2018
Ule & Blencowe, Mol Cell, 2019

Ljubljana Lab

Klara Kuret

Tajda Klobučar

Urška Janjoš

Anja Trupej

Žiga Vičič

Aniela Skrzypczyk

Maksimiljan Adamek

Jure Rebselj

Jona Novljan

Taja Valovec

Klara Kuret, visiting student since November 2019 and started PhD in 2020, works on computational studies of nuclear RNP condensates.

Tajda Klobučar, PhD student since 2020, studies protein-RNA and RNA-RNA interactions that assemble nuclear RNP condensates, mentored by Miha Modic.

Urška Janjoš, Research assistant since December 2020 and PhD student since 2021, studies the functions of nuclear RNPs that form on retained introns.

Anja Trupej, visiting student since 2020, and then starting PhD in October 2022, works on proximity-based studies of RNP condensates.

Žiga Vičič, Research assistant since October 2021, works on iCLIP, ribosome profiling and molecular biology.

Aniela Skrzypczyk, postdoc since April 2022, studies mechanisms of RNA condensates in neuronal differentiation.

Maksimiljan Adamek, PhD student since 2022, works on biochemistry and structural studies of protein-RNA complexes.

Jure Rebselj, visiting student since Sept 2022, focusing on computational biology.

Jona Novljan, visiting student since Dec 2022, focusing on high-throughput studies of RNP assembly and function on specific RNAs.

Taja Vatovec, visiting student Jan-Apr 2023, working with Urška on retained introns.

more at ulelab.info

Thank you!

THE FRANCIS CRICK INSTITUTE

KEMIJSKI INŠTITUT

erc
European Research Council
Established by the European Commission

wellcome

mnda
motor neurone disease association

This project has received funding from the European Research Council (ERC) under the European Union's Seventh Framework Programme (617837-Translate) and Horizon 2020 research and innovation programme (835300-RNPdynamics)

UK Dementia Research Institute

KING'S College LONDON

UKRI Medical Research Council

Alzheimer's Society

Alzheimer's Research UK

Donirajte del dohodnine ASEFu

- **1% dohodnine** za financiranje upravičencev do donacij.
- Donacija dela dohodnine vas **ne stane nič**.
- Zadnji rok je **31. december 2023**.

Kako oddati zahtevek:

1. **Elektronsko** prek portala eDavki.
   - Vloga "Zahteva za namenitev dela dohodnine za donacije (Doh-Don)".
   - V vlogi vpišite naziv organizacije (Inštitut ASEF),
   - davčno številko (84740175) in
   - višino odstotka, ki ga namenjate (0,1, %, 0,2 %, … 1%).
2. Osebno ali po pošti pri pristojnem finančnem uradu z izpolnjevanjem **fizične kopije dokumenta.** Dokument lahko dobite danes pri nas.

Z vašo donacijo bo ASEF lahko še dalje omogočal nove priložnosti za mlade talente in povezoval Slovenijo s svetom.