LiFTS

Li-Fraumeni over Time Study

UK LFS 2024
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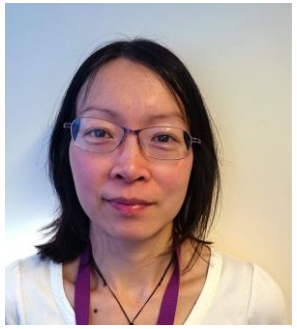

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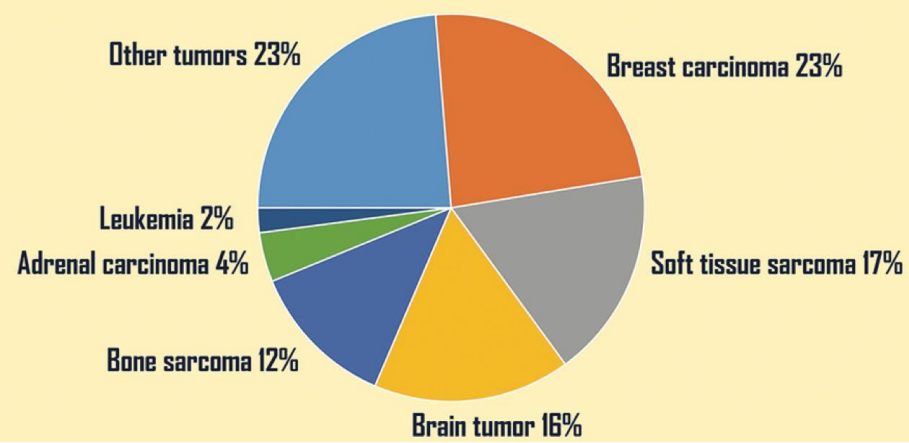
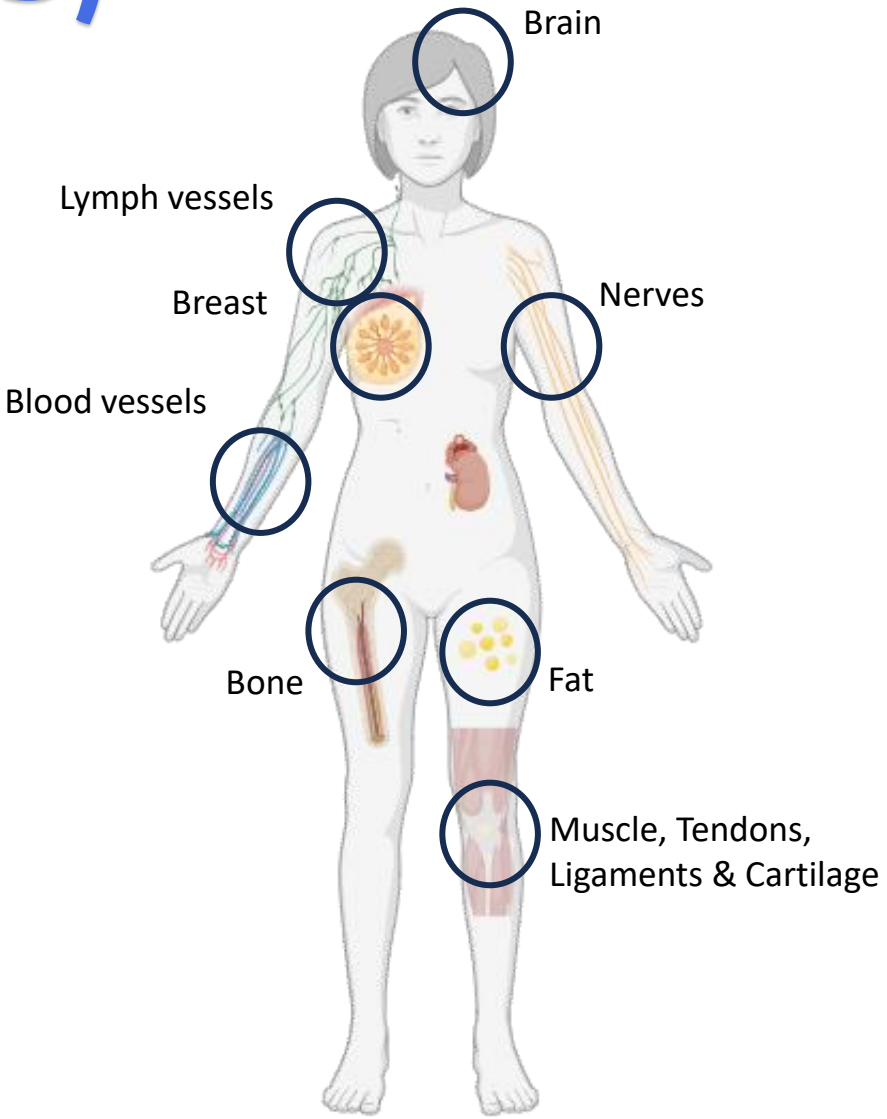
Li Fraumeni syndrome (LFS)

- Increased lifetime risk of cancer
- Autosomal dominant inheritance
- Variable across individuals (even in the same family)
- Early onset of cancer is common
- Some association between particular genetic changes that may modify cancer risk and type

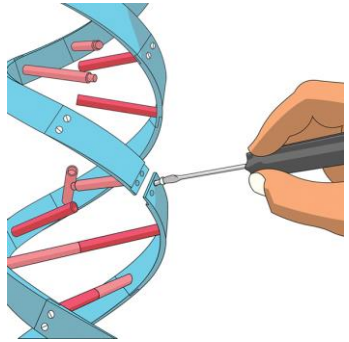


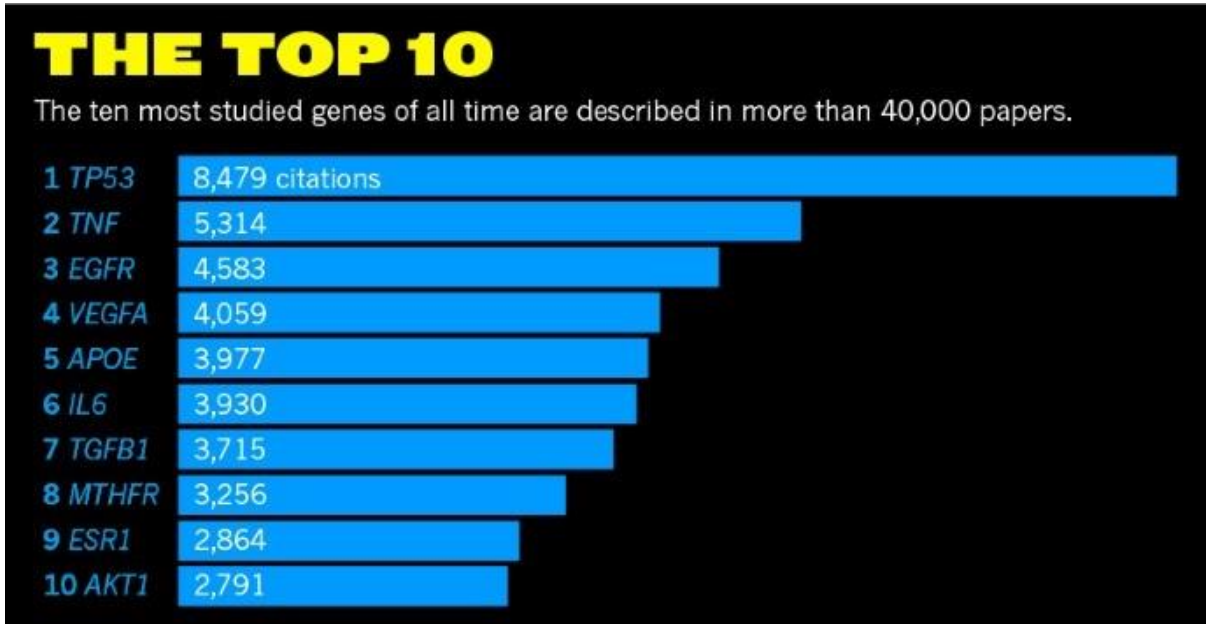


The most studied gene of all time

TP53 is a tumour suppressor gene, and widely known as the “guardian of the genome”.

It is mutated in roughly half of all human cancers.





“There is no gene more important than *TP53*”

Bert Vogelstein.

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Yet … we still understand very little about:

- Why are some cancer types more frequent than others in people with LFS as compared to general population?
- What factors determine risk of cancer across individuals with different mutations in *TP53*? Why is this risk variable in the first place?
- How does mutation of *TP53* affect cells across different organs?
- How to predict cancer risk to improve personalised management of LFS individuals?

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What determines cancer risk in different organs?

We think that mutant patches develop and behave differently in the organs of people with LFS. It is this difference in the mutant patch behaviour that determines why some organs in people with LFS have a higher risk of developing cancer than in other organs. However, we do not know why this is.

As a result, it is challenging to:

- predict each individual's cancer risk,

- design effective early detection programmes,

- or discover LFS specific cancer treatments.

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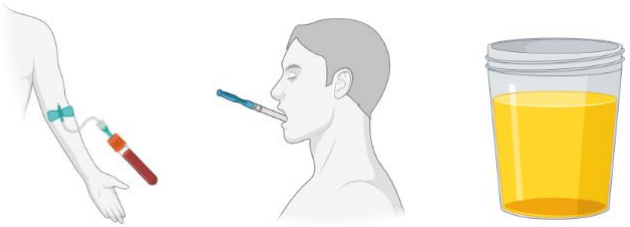
Three ways we can study mutant patches in LFS through LiFTS

1

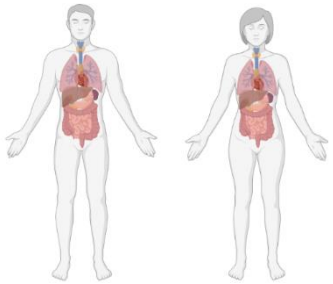


Collect samples (such as blood, saliva/cheek swabs, semen, and urine) at 6-12 month intervals

2

Collect and freeze samples from biopsies (such as colon) and tumours after they have been removed. In Cambridge we are now able to do skin biopsies for research purposes.

3



Facilitate organ donation for people with LFS

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Recurrence risk

- For some families, a *TP53* mutation can arise in a family member for the first time. This is known as a ***de novo* mutation**.
- In families where this is the case, it is hard to give an accurate prediction of the chance of future pregnancies inheriting the *TP53* mutation and being affected by LFS. This is known as **recurrence risk**.
- By also applying Nano-seq to sperm samples from the fathers of *de novo* cases, we can develop a **more accurate test** for estimating recurrence risk.

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Benefits of participation in LiFTS

- There is potential to identify early cancer transformation which would be discussed with your clinical team, if found.
- This study could assist in developing new surveillance and treatment strategies for people with LFS.
- For the families in which there is a *de novo* mutation, we can provide an estimate of recurrence risk from the father's sperm.

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Would you like to be involved?

1. Contact us at: lifts@tp53.org.uk (no commitment, just to state an interest)
    1. **You can be involved in our study as well as others and it is open to anyone with a diagnosis of LFS or LFS-like syndrome.**
2. Initial introduction and consent conversation (can be done by telephone + post)
3. Send out packs to you at home (for collection of cheek swabs, sperm, and urine) – new packs every 6-12 months
    1. Sample collection done at home and posted back to our lab in Cambridge
4. Visit one of our Recruitment Hospitals for a blood sample (currently Cambridge for adults and GOSH for children (and their parents) but actively expanding our network at present) – every 6-12 months
5. Please let us know if you have any procedures such as a colonoscopy or biopsy so we can co-ordinate transfer of (surplus) tissue

Cambridge LFS research clinic

- Dedicated research clinic in Cambridge for individuals with LFS
- Also recruiting individuals with other genetic conditions including cancer predisposition
- Through this clinic we are able to arrange:
  - Blood sampling
  - Cheek (buccal) swabs
  - Urine sampling
  - Research skin biopsies
- If you would like to attend, please contact our team either on: lifts@tp53.org.uk or joseph.christopher1@nhs.net

NIHR | Cambridge Clinical Research Facility

What we aim to achieve?

- Transform our understanding of how mutation of *TP53* affects different organs and how that relates to cancer risk.
- Understand how mutant patches can lead to cancer in people with LFS.
- Identify new ways we can detect and treat LFS-associated cancer.

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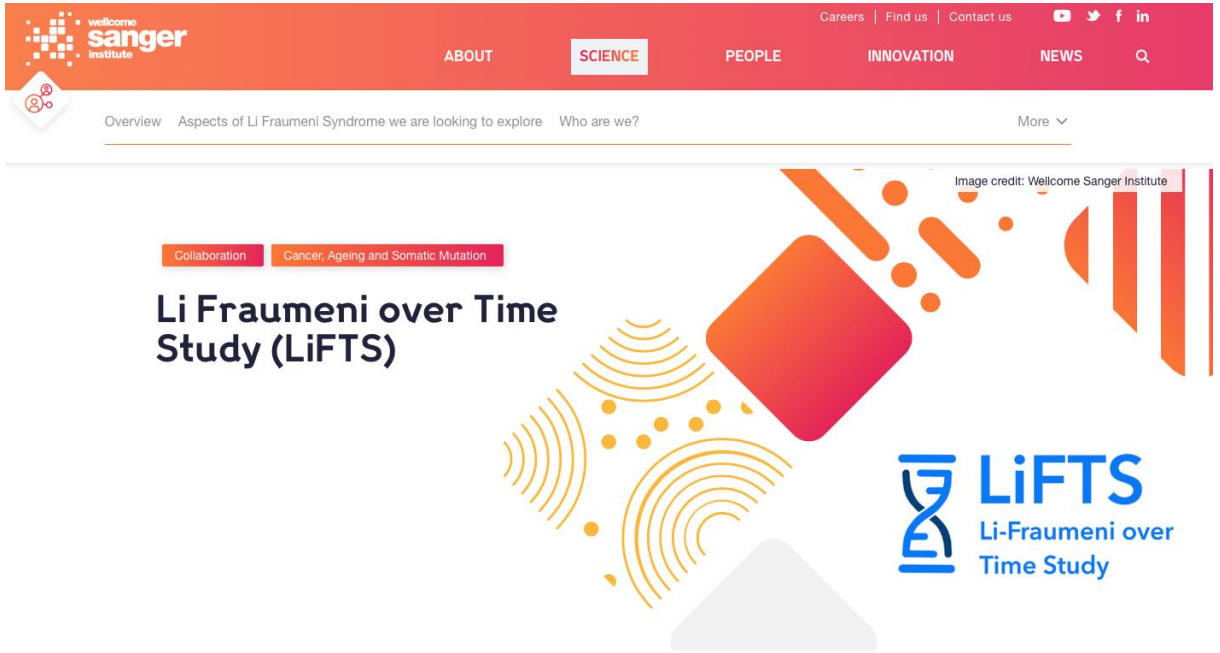
How to contact us?

Please contact us by sending an email to: lifts@tp53.org.uk

For more information visit our website:



Acknowledgments

Thank you to all the Participants!

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