IMPERIAL

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SAPPHIRE: Cracking The Code Of Fatty Protein Modifications To Advance Cancer Research

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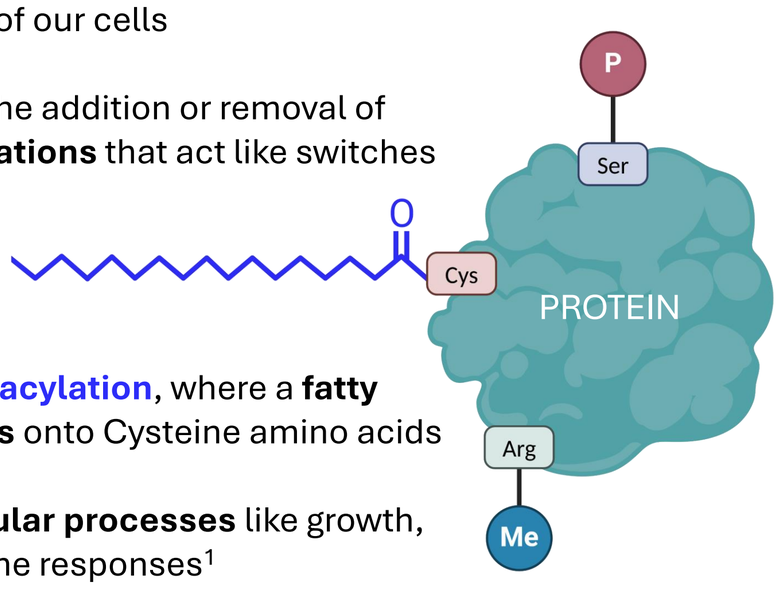
STEM for BRITAIN

BACKGROUND

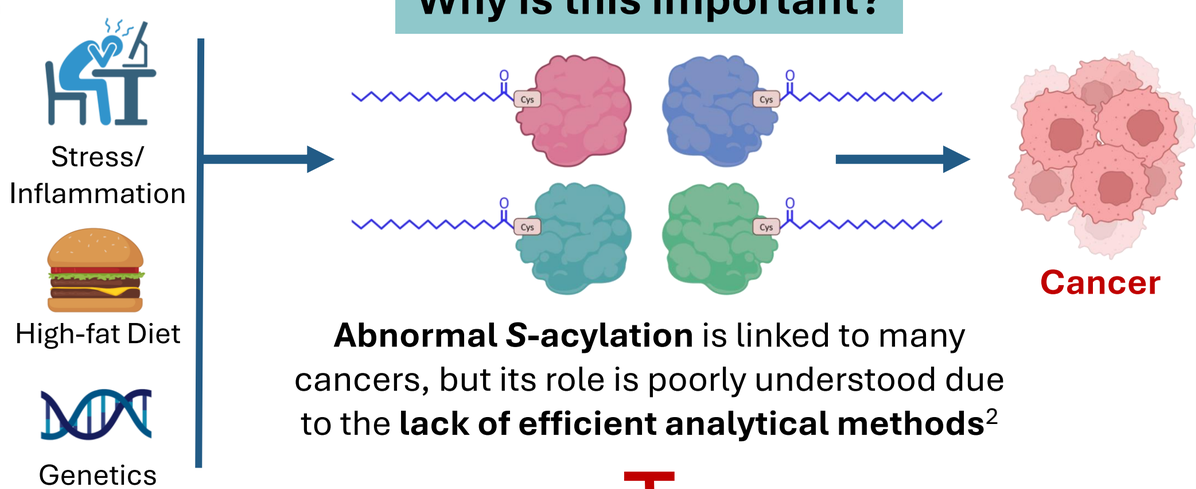
What are fatty modifications?

- Proteins are the **workforce** of our cells
- Their functions depend on the addition or removal of different **chemical modifications** that act like switches



- One such modification is **S-acylation**, where a **fatty acid is attached to proteins** onto Cysteine amino acids
- *S*-acylation **fine-tunes cellular processes** like growth, communication, and immune responses[1]

Why is this important?



Abnormal *S*-acylation is linked to many cancers, but its role is poorly understood due to the **lack of efficient analytical methods**[2]

To develop effective **cancer therapies**, we need **innovative tools to study *S*-acylation in cells and tumours**

OUR TECHNOLOGY

The problem

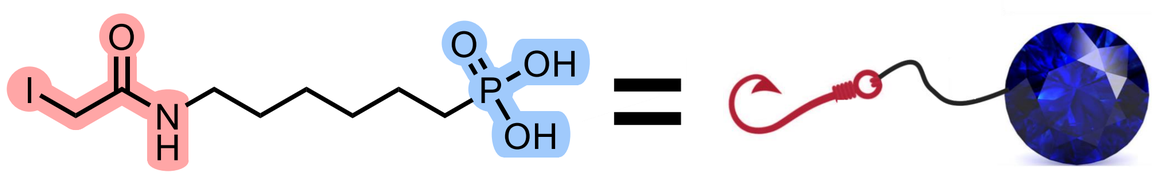
S-acylation is **highly hydrophobic** and cannot be analysed directly by standard instrumentation. Its detection requires complex workflows (e.g., ABE, acyl-RAC, metabolic labelling), which suffer from:

- **Low specificity -** false positives
- **Poor Cys site identification**
- **Low throughput** - laborious
- **Inapplicability to tumour analysis**

These challenges limit our ability to identify *S*-acylation biomarkers and drug targets in cancer[3]

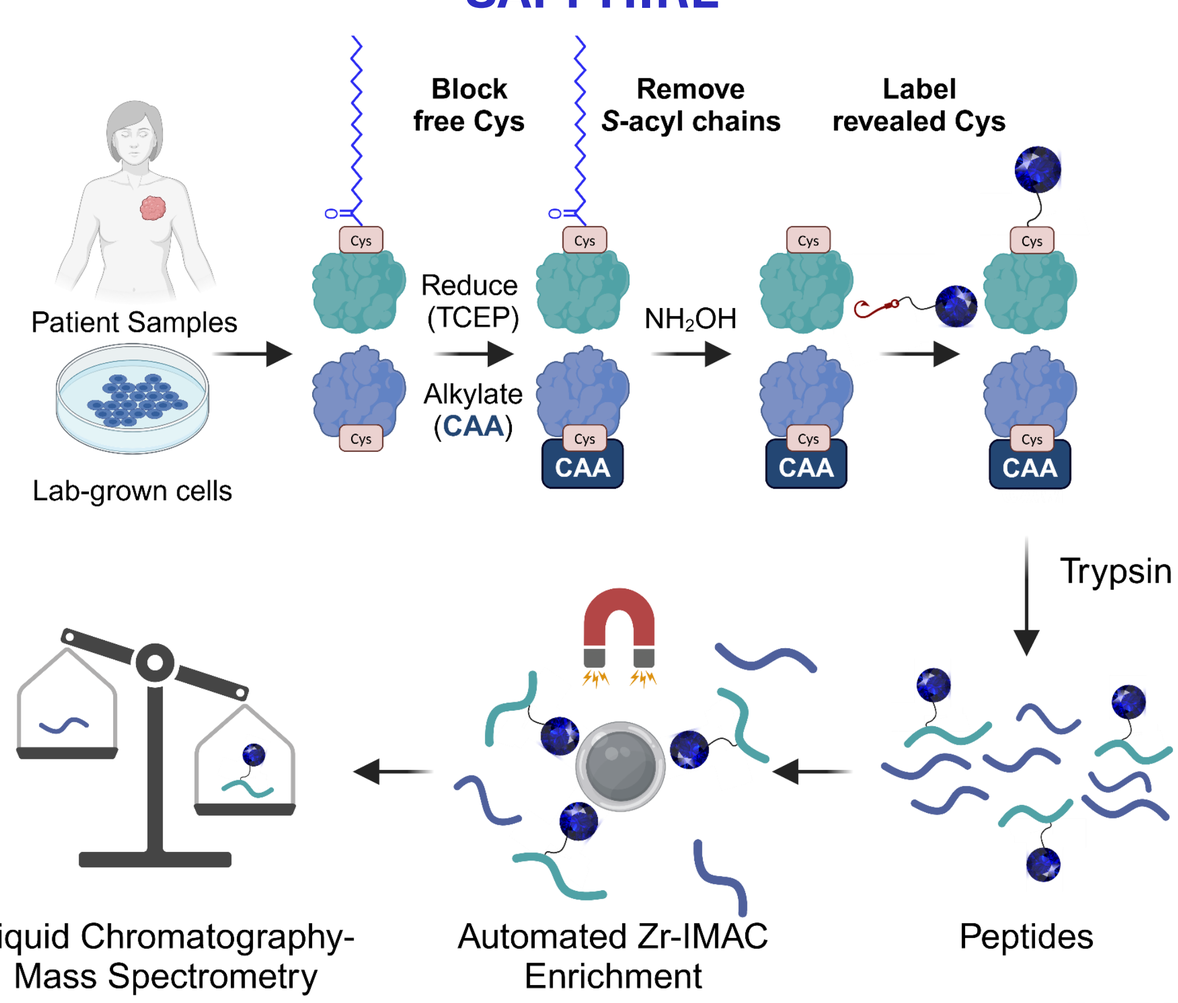
Our solution

We developed a **novel method for sensitive analysis of *S*-acylation** by using a **chemical probe**[4] that specifically labels *S*-acylated proteins



S-**A**cylation **P**rofiling by **PH**osphonate tagg**I**ng p**R**ot**E**omics (**SAPPHIRE**)

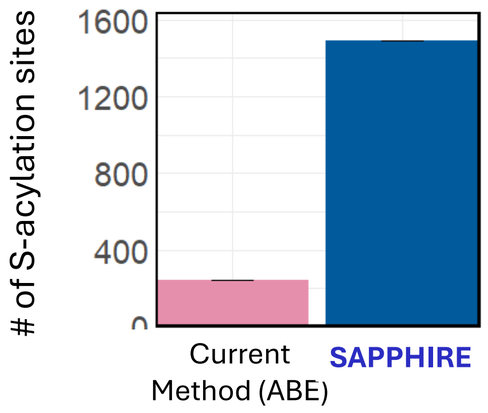
SAPPHIRE



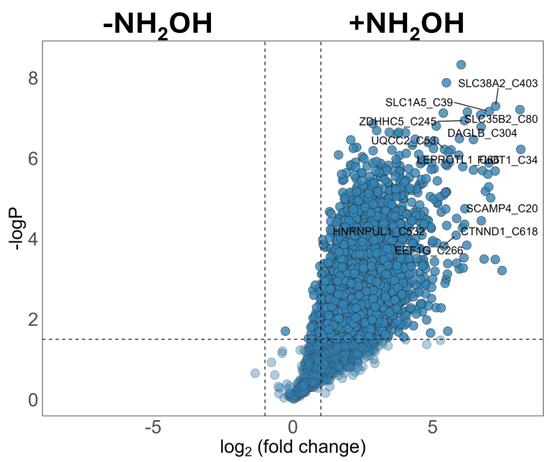
SIGNIFICANCE

Our findings

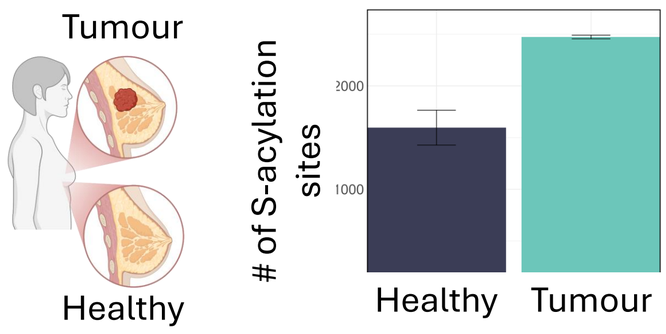
In cancer cells, **SAPPHIRE outperforms existing methods by 400%**



SAPPHIRE is ultra-specific, with zero identifications in the control condition



SAPPHIRE enabled **unprecedented analysis** of *S*-acylation patterns in human tumour samples



- **Twice as much *S*-acylation in Breast Cancer vs Healthy tissue from the same patient**
- Identified *FASN1* and *CTNNB1* proteins (cancer biomarkers) are *S*-acylated in Tumour only, highlighting SAPPHIRE's potential for new **biomarker discovery**

Advantages of SAPPHIRE

- **High specificity**
- **High-throughput** – 96-well plate
- **Semi-automatable**, easy workflow
- **Applicable to all biological samples**
- **Cost-efficient**

Future Outlook

SAPPHIRE will be used:

To test hits from ongoing **Drug Discovery Campaigns**

For **Biomarker Discovery** in the clinic

As a **Research Tool** in labs

References and Acknowledgements:
1. S. Mesquita, F. *et al.* Nat. Rev. Mol. Cell Biol. 2024 256 25, 488–509 (2024).
2. Tate, E. W. *et al.* Nat. Rev. Cancer 2024 244 24, 240–260 (2024).
3. Wang, Y. & Yang, W. J. Proteome Res. 20, 14–26 (2021).
4. Liu, X. *et al.* J. Proteome Res. 22, 1270–1279 (2023)
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