UNIVERSITY OF BIRMINGHAM

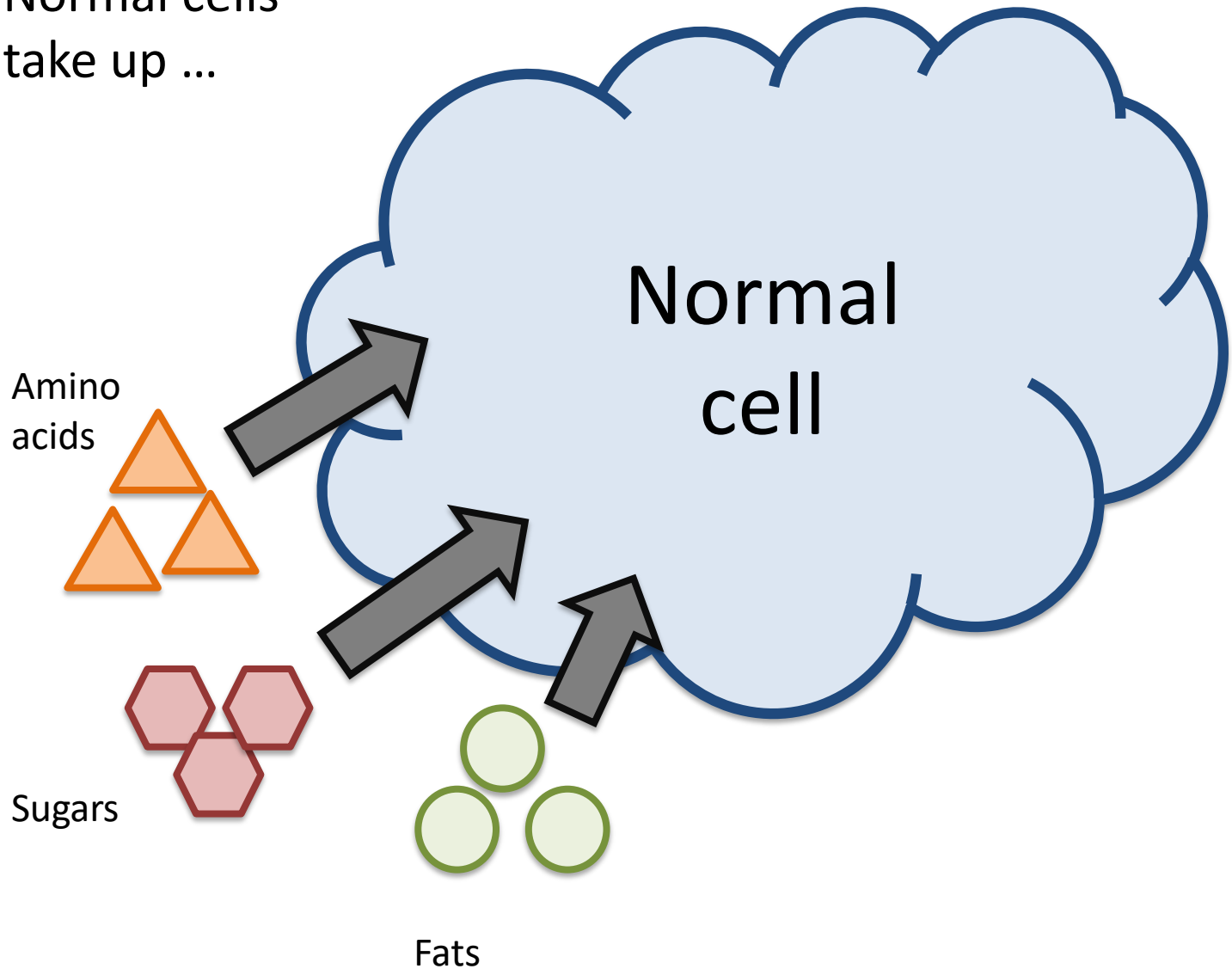
INSTITUTE OF CANCER AND GENOMIC SCIENCES

Project update: Examining the metabolism of paediatric brain tumours using mass spectrometry

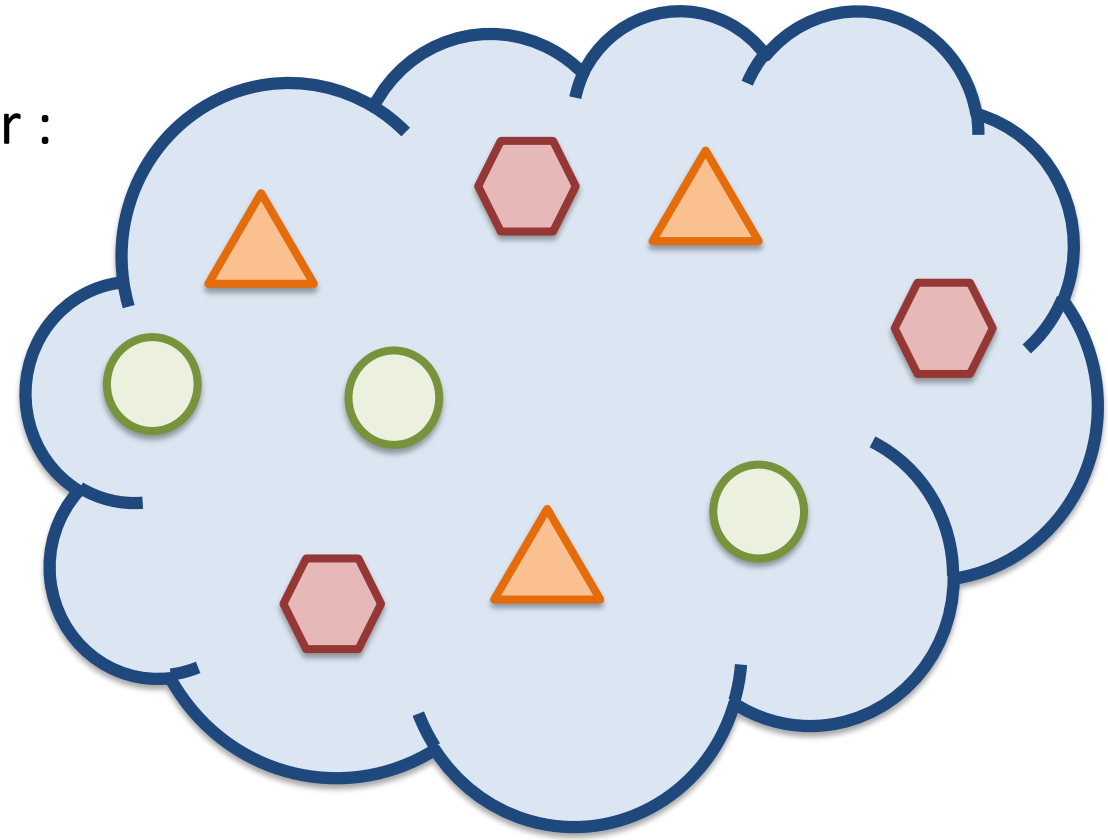
Christopher Bennett

21/06/2019

Normal cells take up …



And a normal cell will use the resources for :

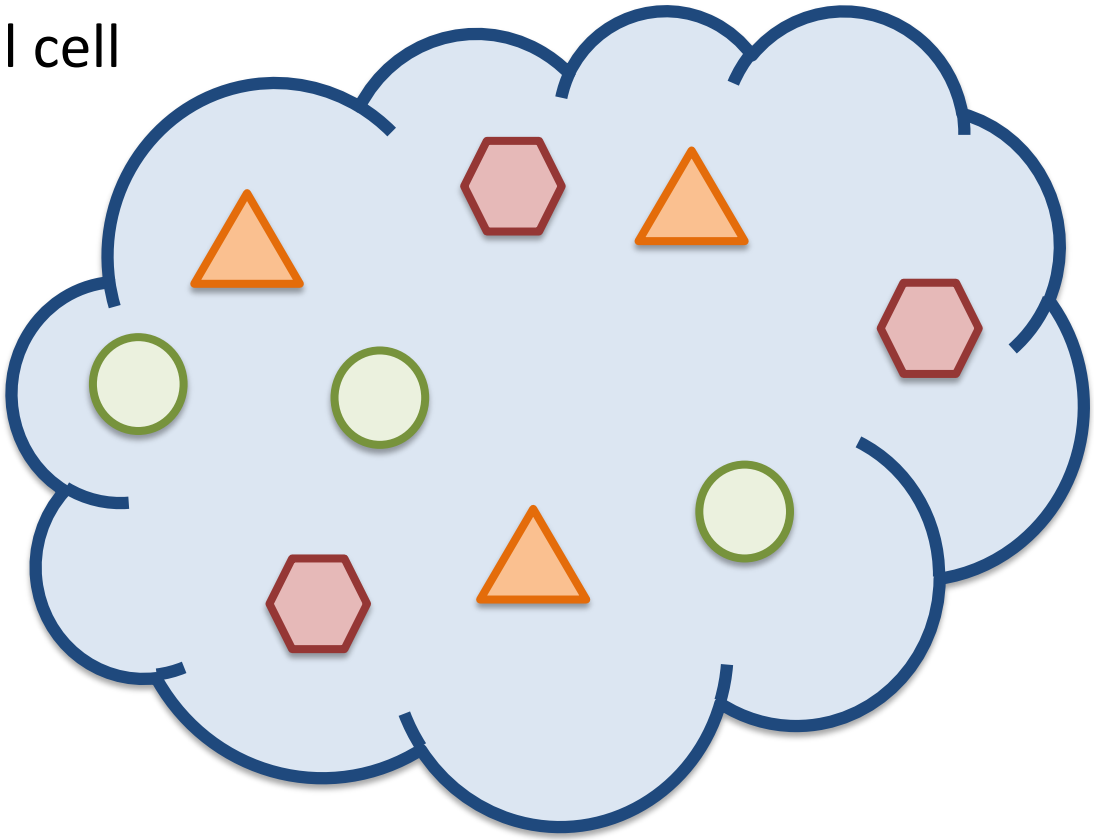


1. Cell maintenance

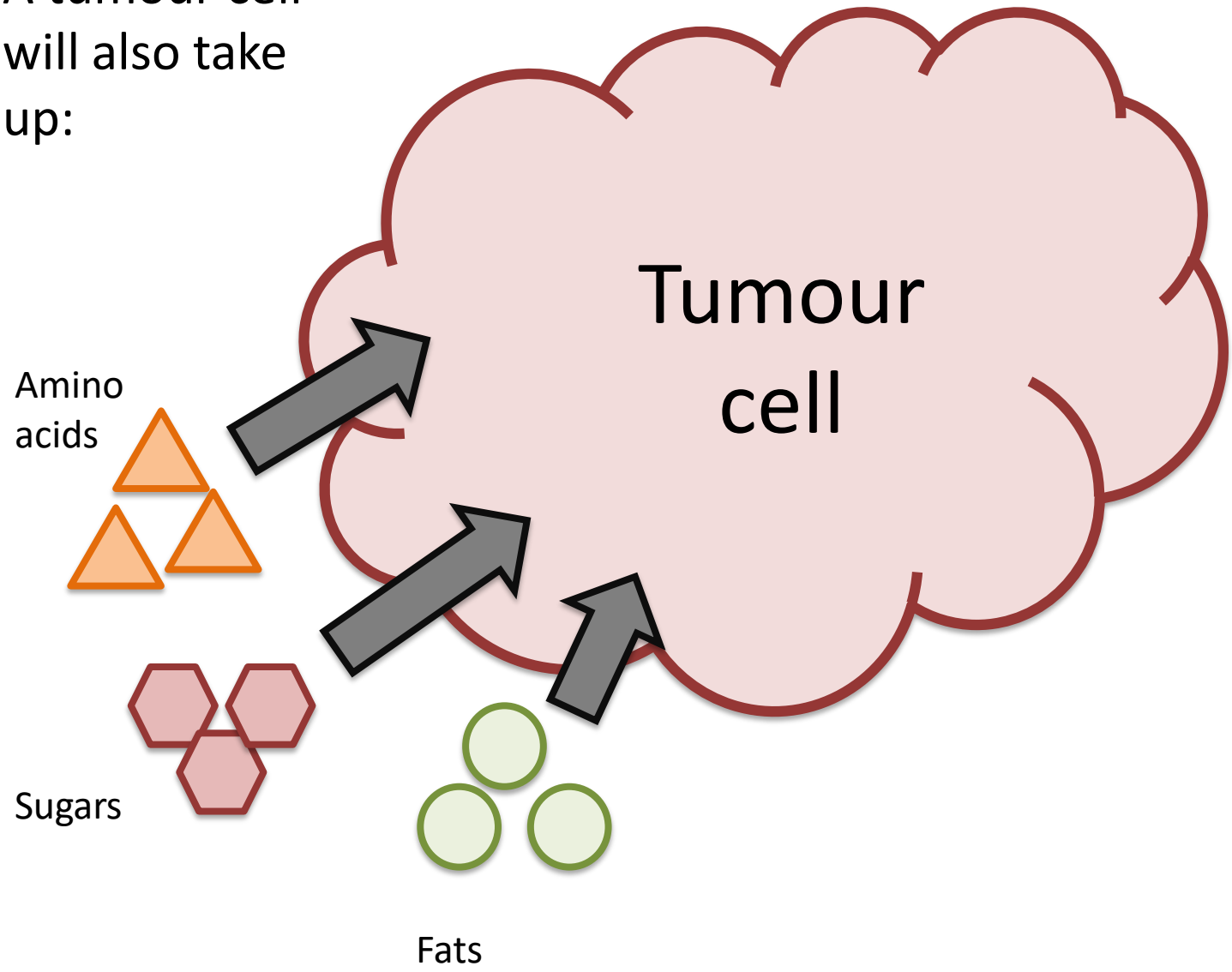
2. Efficient energy production

3. Performing specialised functions

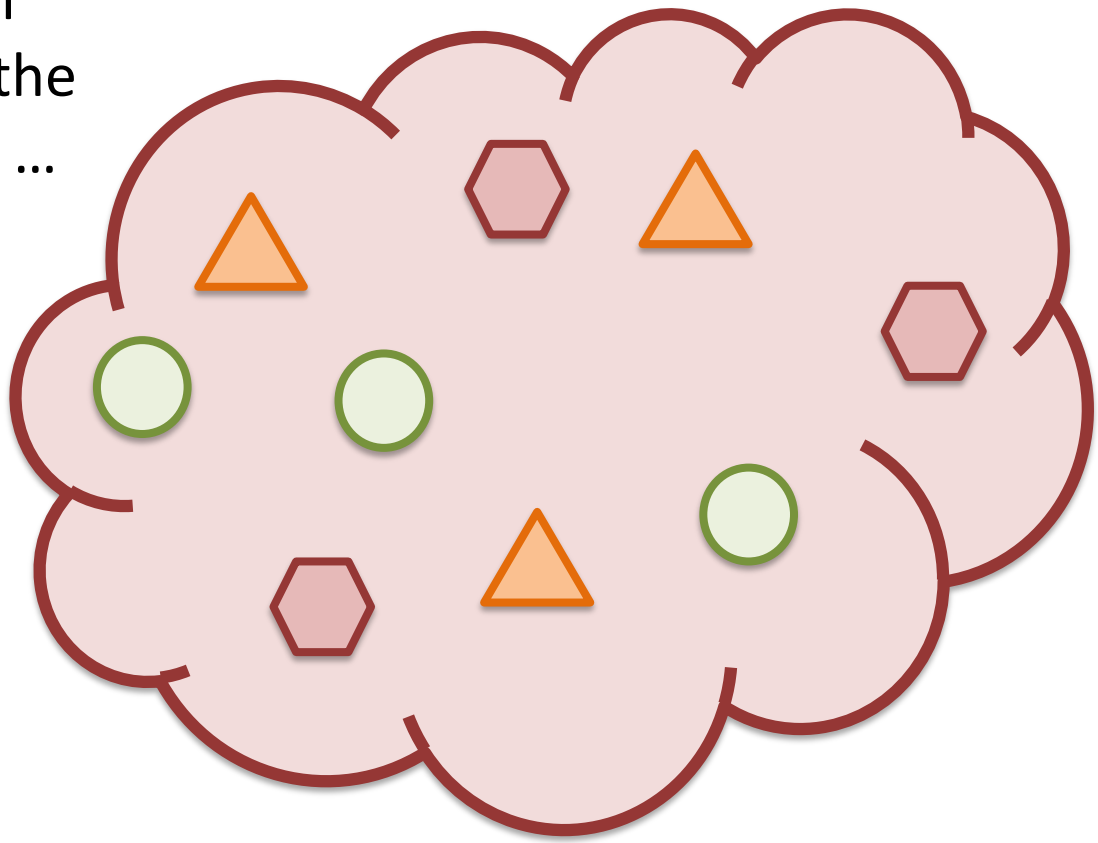
And remains a
single normal cell



A tumour cell will also take up:



But a tumour cell will use the resources to …



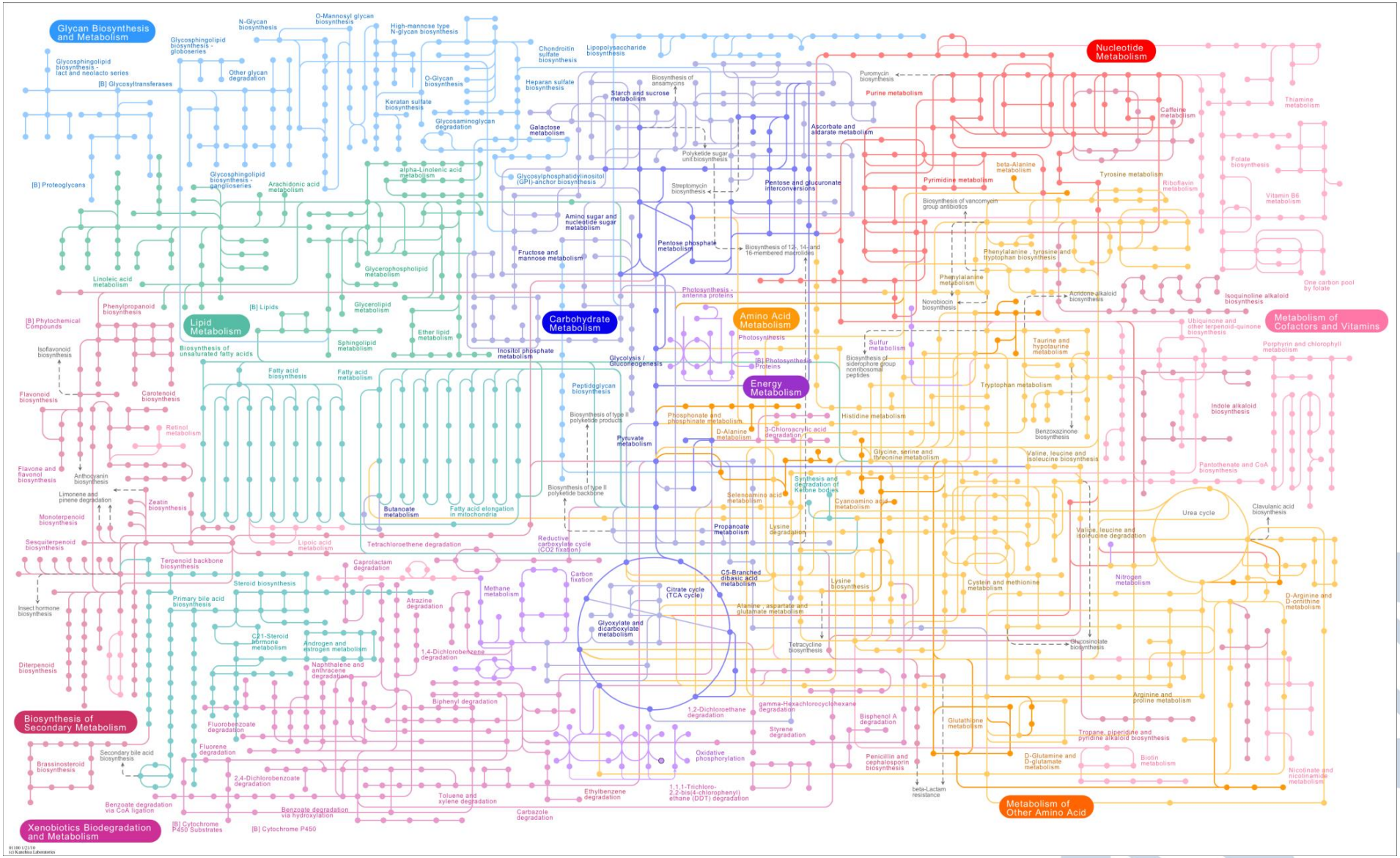
Build new cellular components

And so a tumour cell will divide …

And divide …

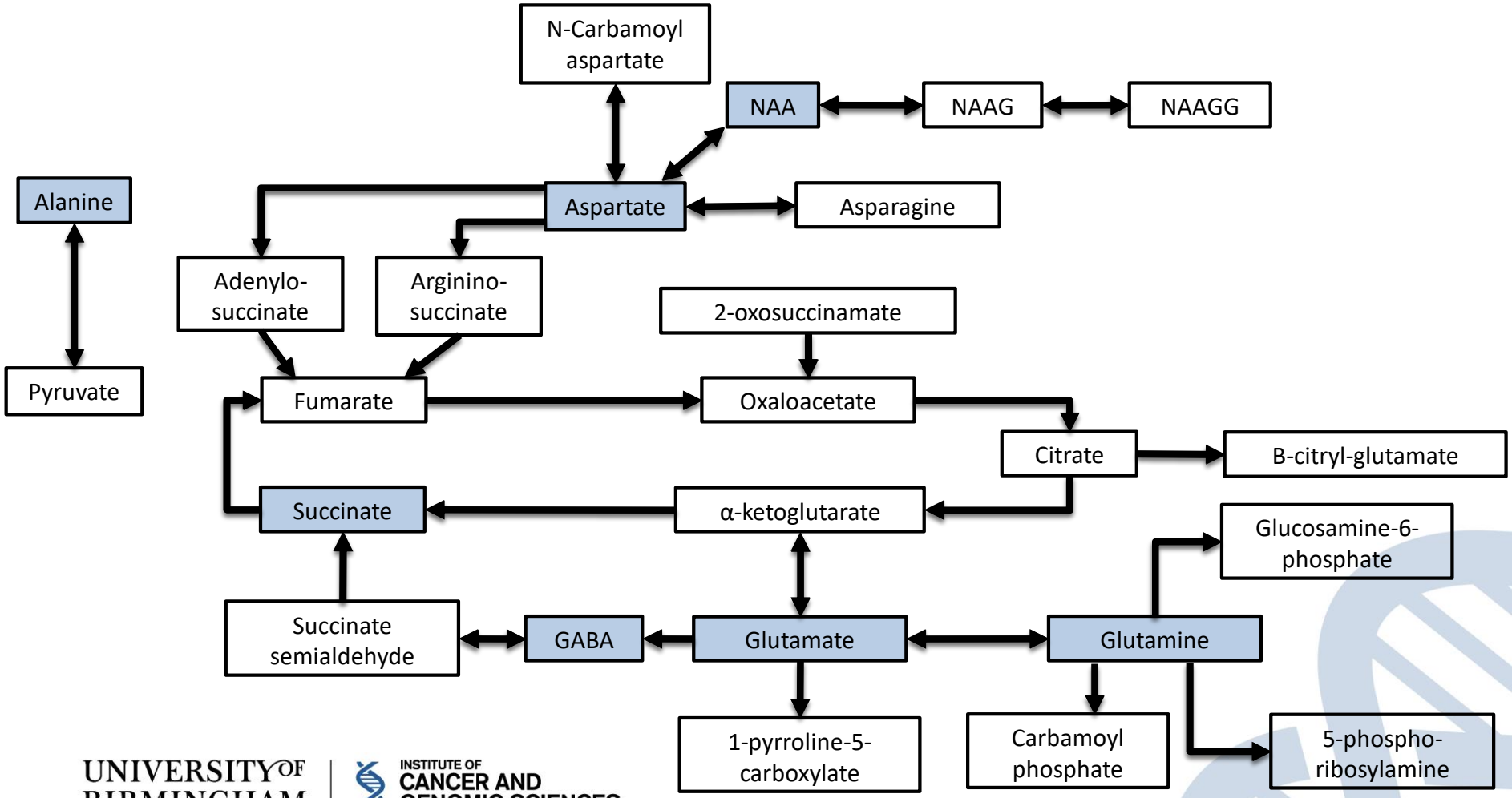
And divide, forming a tumour

Metabolism is complex. Below is a “map” of metabolism, where each dot is a chemical (known as a metabolite), and each line is a possible chemical reaction a cell can perform:



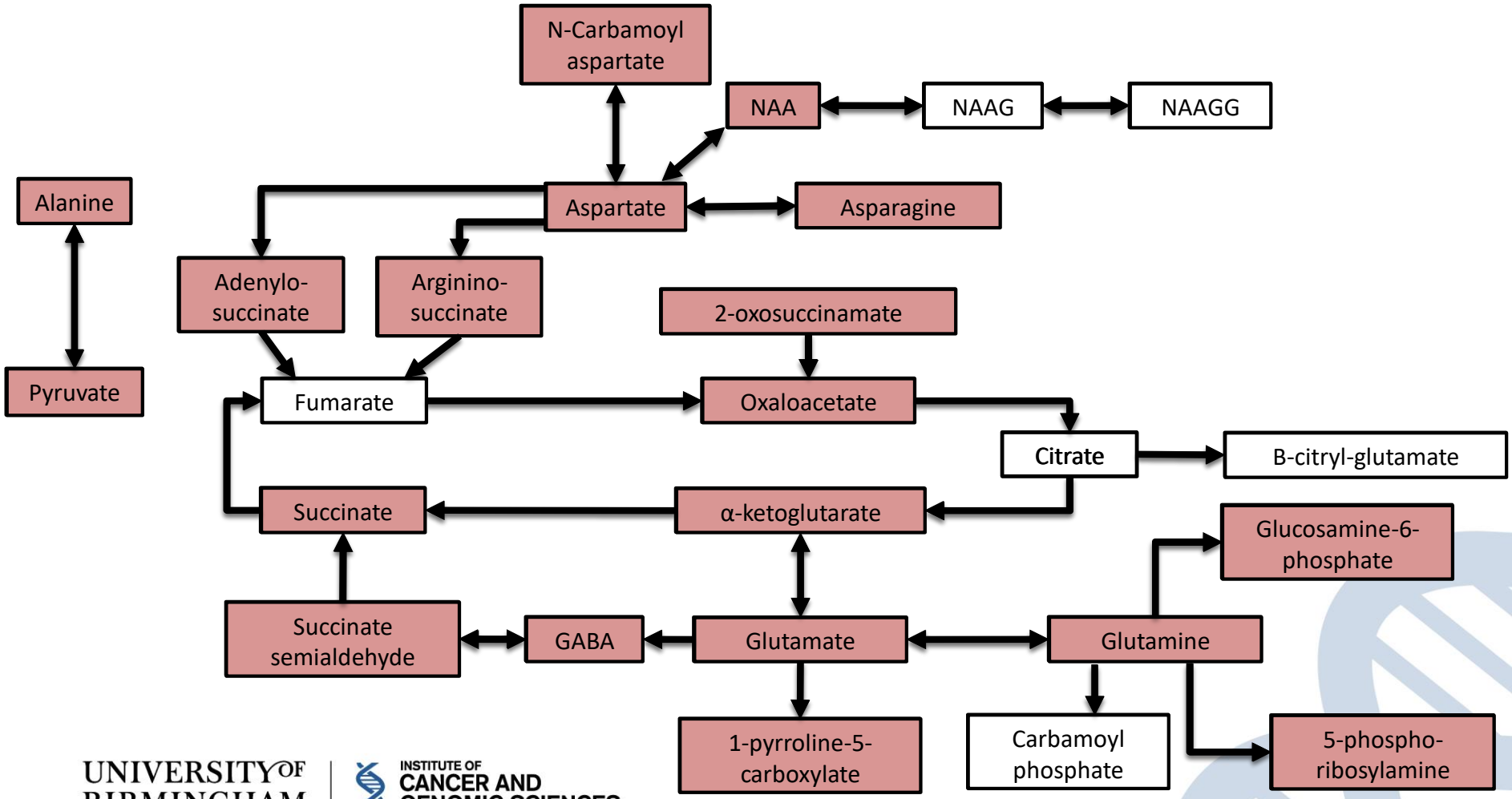
Our previous experiments, using Magnetic Resonance Spectroscopy, are limited in the number of detectable metabolites. Below is an example of a metabolic pathway, with detectable metabolites highlighted in blue.

With only a few metabolites we are not able to accurately describe how tumours use metabolites.



UNIVERSITY OF BIRMINGHAM | INSTITUTE OF CANCER AND GENOMIC SCIENCES

Mass spectrometry is another technique that can detect metabolites. For the same pathway as before, mass spectrometry can detect all the metabolites highlighted in red. This extra information is useful for showing differences in tumour metabolism.

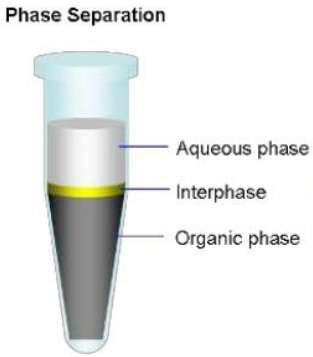


UNIVERSITY OF BIRMINGHAM | INSTITUTE OF CANCER AND GENOMIC SCIENCES

Methods

- Cohort included 60 samples with previously acquired magnetic resonance spectroscopic data.
  - 16 ependymoma (EP), 24 medulloblastoma, 20 pilocytic astrocytoma (PA). Total of 60 cases.

Tumour sample



Metabolites extracted from tumour tissue.

- Aqueous phase contains water soluble metabolites like sugars and amino acids.
- Organic phase contains fats (lipids).

Larger samples

Smaller samples

Mass spectrometer

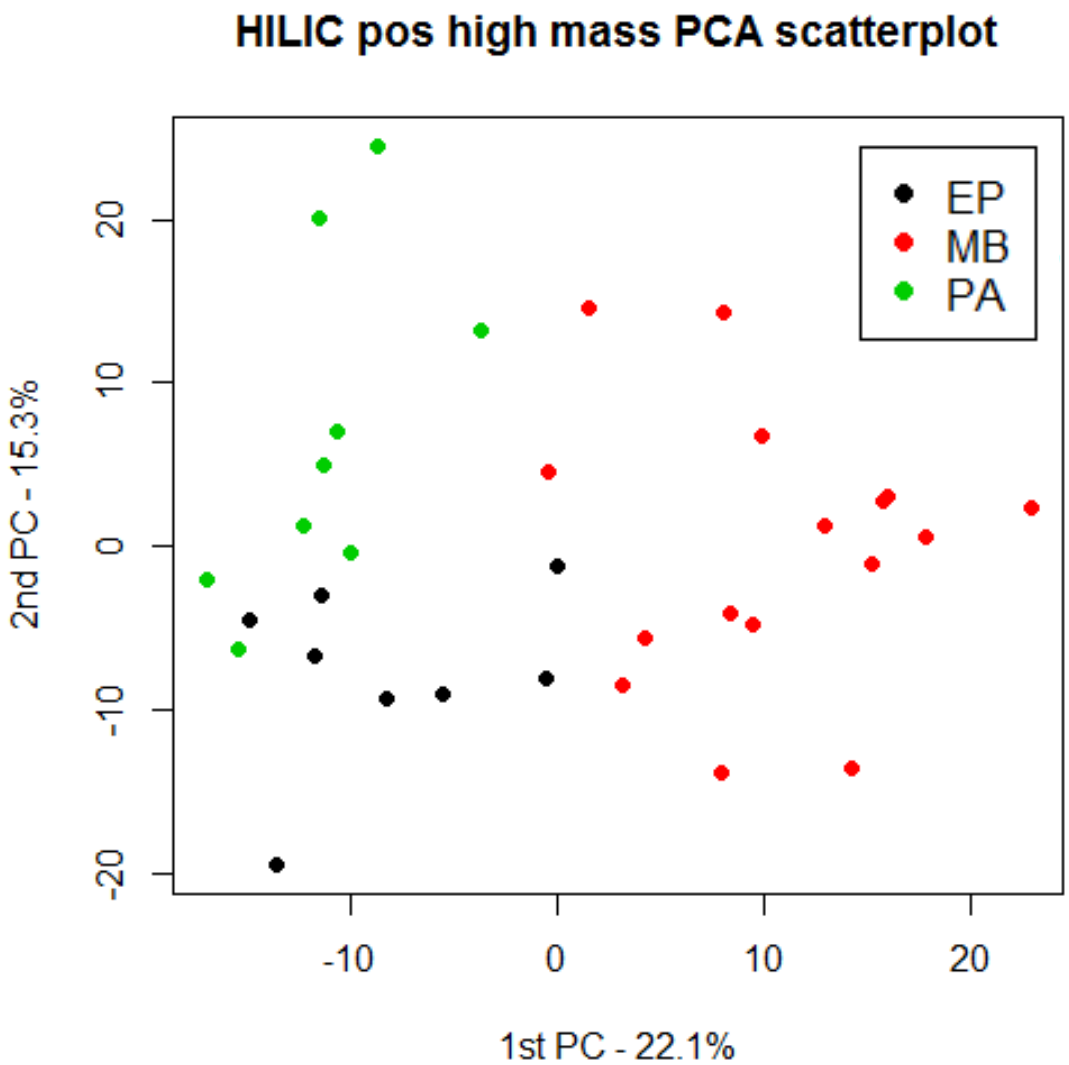
Analysis

Mummichog

Fundulus heteroclitus

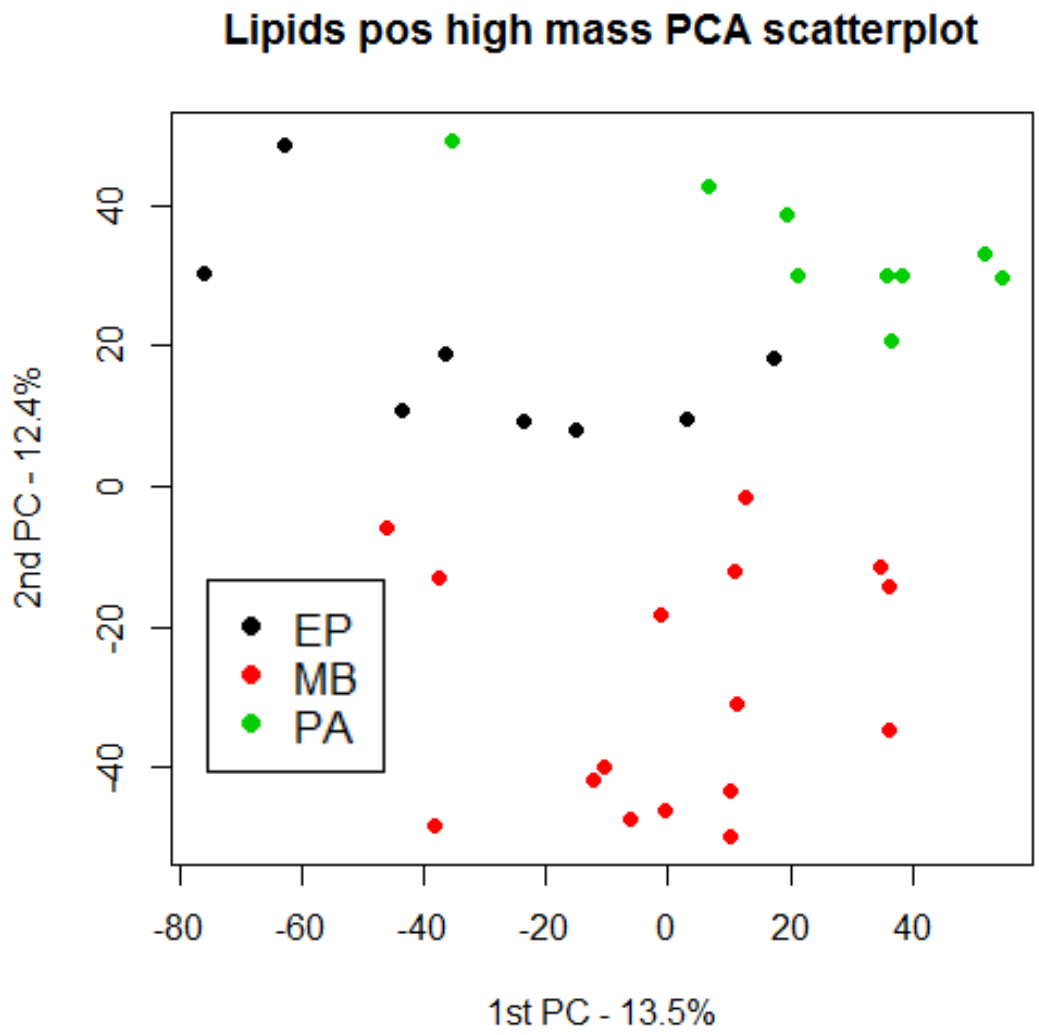
UNIVERSITY OF BIRMINGHAM | INSTITUTE OF CANCER AND GENOMIC SCIENCES

Principal component analysis (PCA) shows which samples are most similar to each other. In this figure we see that tumours of the same type tend to be more similar to each other than to those of other tumour types. These samples are in the large mass cohort, analysed in positive ionisation mode, detecting water soluble metabolites.



UNIVERSITY OF BIRMINGHAM

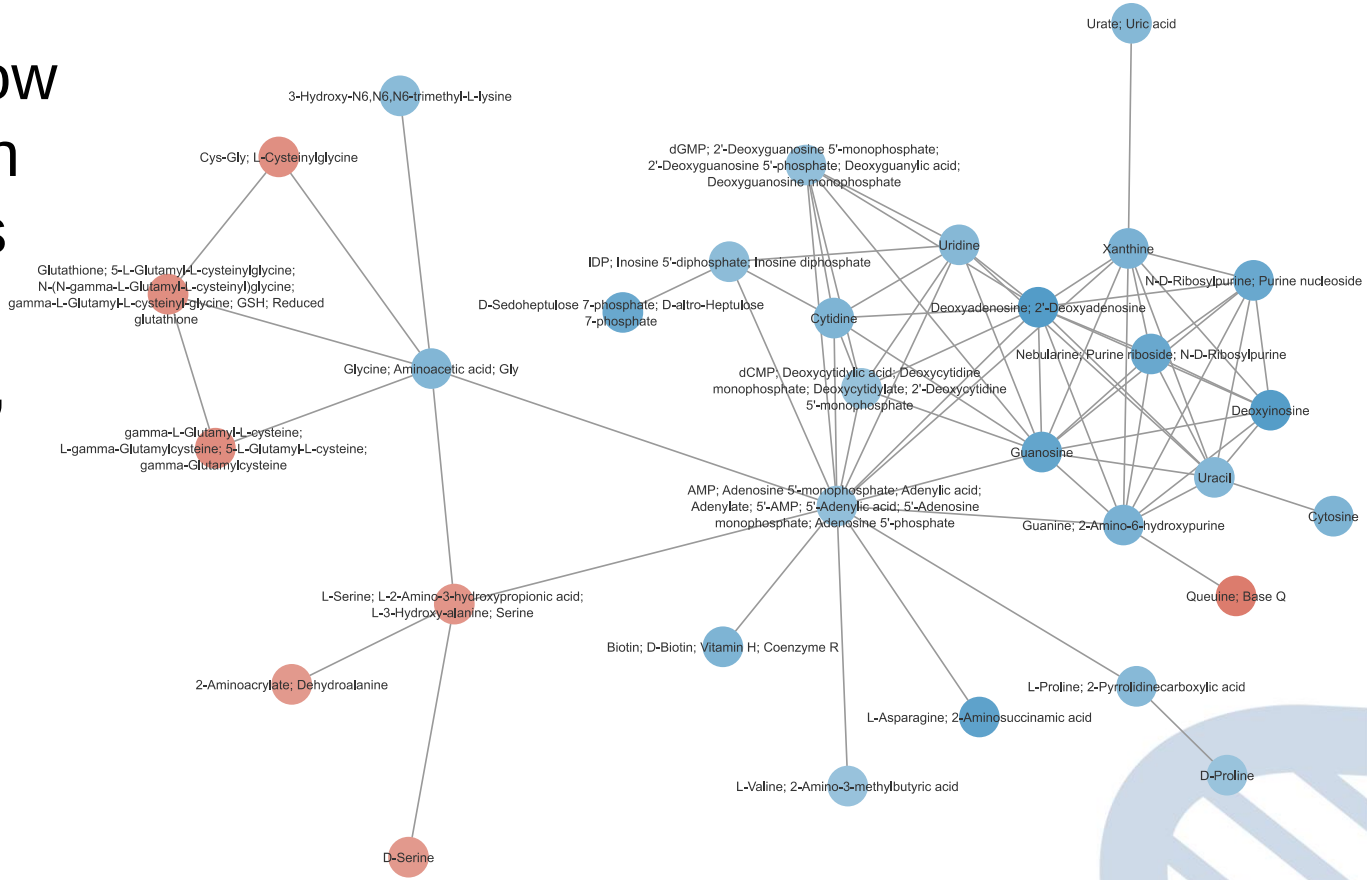
The same is seen when PCA is performed on the lipid data from the same samples in the same ionisation mode.



UNIVERSITY OF BIRMINGHAM

Results – pathway analysis

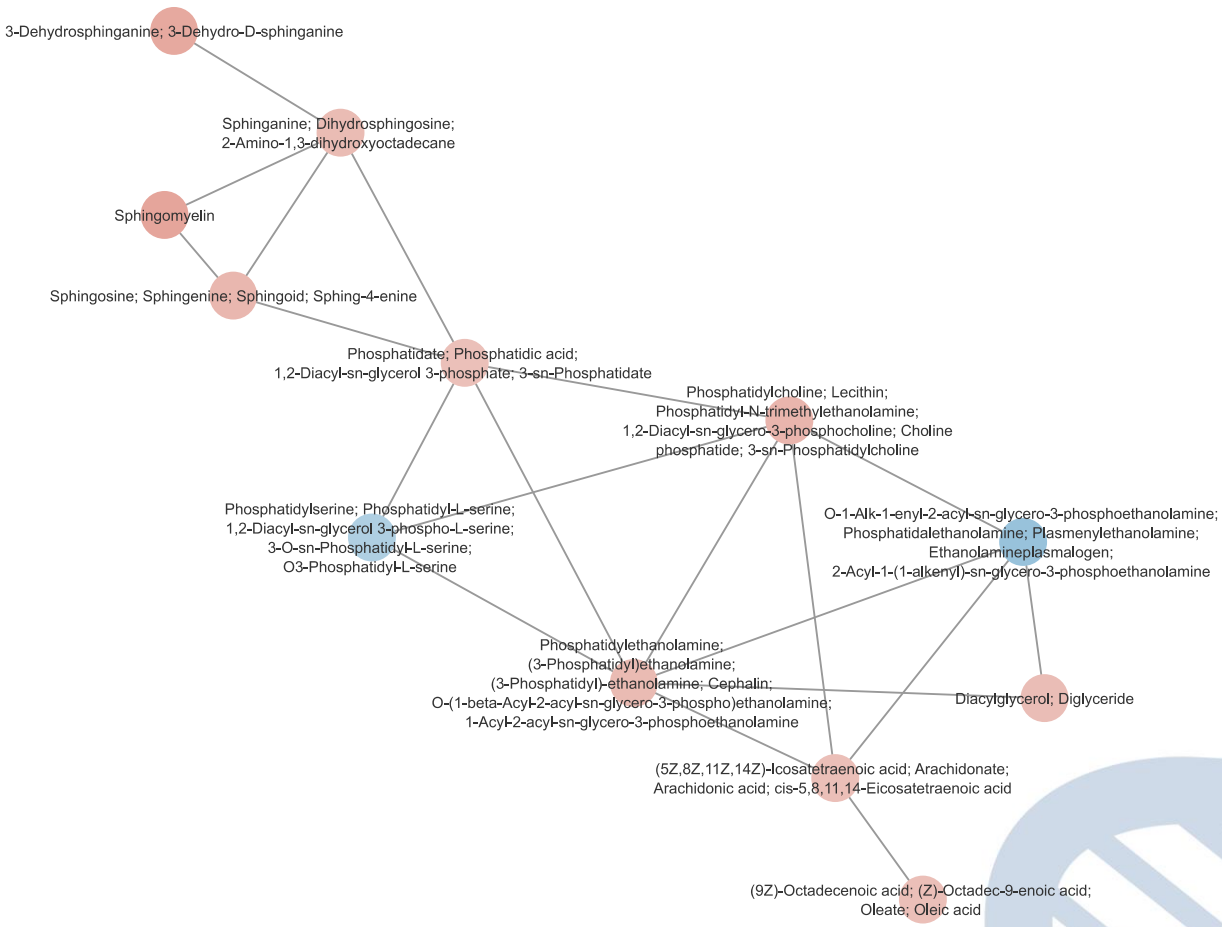
- Tumours show differences in how tumours make DNA components, use some amino acids and sugar molecules.



UNIVERSITY OF BIRMINGHAM | INSTITUTE OF CANCER AND GENOMIC SCIENCES

Results – pathway analysis

- Tumours also show differences in membrane components and signalling lipids.



Conclusions

- Mass spectrometry can identify >3000 features.
- Pathway analyses identifies potential therapeutic targets.
- Mass spectrometry is able to provide data on lipid metabolism.

Future work

- A more in depth analysis of the data to examine each tumours metabolism.

- Addition of more samples
  - Medulloblastoma
  - Low grade gliomas