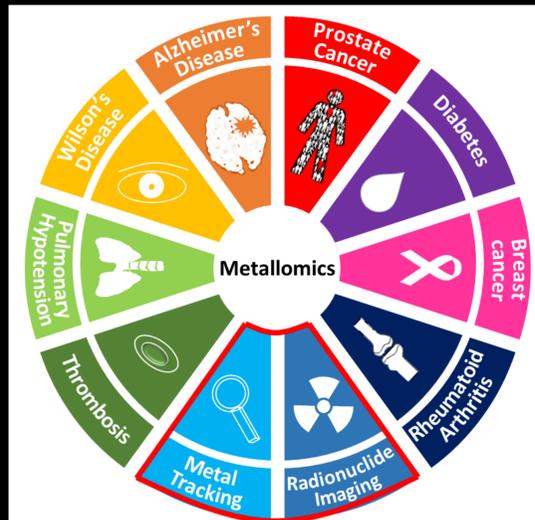


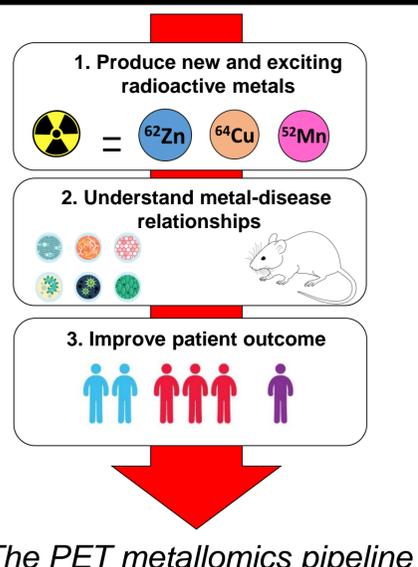
# P.E.T. METALLOMICS – USING RADIOACTIVITY TO TRACK ESSENTIAL TRACE METALS IN THE BODY

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Metals in health and disease

- P.E.T. metallomics uses radioactive isotopes of metals to **track metals** in the human body without the need for invasive biopsies.
- Metals such as copper (Cu), zinc (Zn) and manganese (Mn) are found naturally in our body and are essential to human health. Too much of these metals, from environmental exposure, or too little, from nutritional deficiency, can have detrimental effects.
- An abnormal balance of these metals has been associated with diseases including **Alzheimer's disease**, **prostate cancer** and **diabetes**. However these changes are poorly understood.
- We have developed methods to produce an exciting range of radioactive metals. This allow us to study metals in humans and animals by **P.E.T. imaging** to improve our understanding of their role in health and disease.



The PET metallomics pipeline

## Following intravenous injection, metals localise to organs that require them to function

### Zinc

**<sup>62</sup>Zn**

- Allows the imaging of **diabetes**, **arthritis**, **prostate** and **breast cancer**.

**Locations and associated function:**

- The liver is one of the major organs involved in zinc metabolism.
- Zinc is important in the pancreas where it helps store insulin.
- Zinc is reabsorbed from the urine by the kidney.

Healthy animal

### Copper

**<sup>64</sup>Cu**

- Allows the imaging of **prostate cancer**, **Wilson's** and **Alzheimer's disease**.

**Location and associated function:**

- Proteins found in the serum deliver copper to the liver.
- Copper is excreted through the intestines as faeces.
- Excess copper is excreted through the kidneys and in to the bladder.

Healthy animal

### Manganese

**<sup>52</sup>Mn**

- Allows the imaging of Dementia, lung cancer, manganism and **breast cancer**.

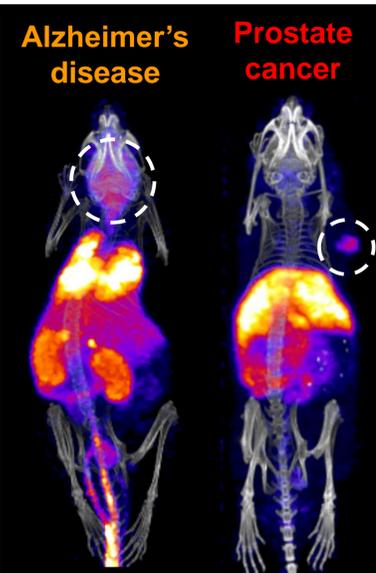
**Location and associated function:**

- The function of manganese in the salivary glands is currently unknown.
- Enzymes found in the heart that are involved in antioxidant defence require manganese.
- Manganese is important for bone development so is seen in the joints.

Healthy animal

## What happens to the normal regulation of metals in disease?

- Many diseases have been associated with altered transport and excretion of trace metals (see "Metals in health and disease" above).
- The prostate gland is associated with the one of the highest concentration of zinc in the body, but in **prostate cancer** zinc levels are significantly lower and copper levels are increased. Whereas **Alzheimer's disease** is thought to have an increase in both zinc and copper levels compared to healthy brain tissue.
- These changes are poorly understood. With **PET metallomics** we can now dynamically **track metals** in models of disease over time. It also allows us to see what happens to these metals following treatment regimes.
- For example, **PET imaging** with <sup>64</sup>Cu shows altered distribution of copper in models of Alzheimer's disease (right) and prostate cancer (far right). Tumours are grown on the back of the mouse using prostate cancer cells.



## The future of PET metallomics is in improving patient outcome

- **Locate** disease
- **Diagnose** and stage disease
- **Predict** response to therapy
- **Monitor** response to therapy

1. Imaging copper in patients with prostate cancer (Righi *et al*)
2. Imaging zinc in patients with Alzheimer's disease (Degrado *et al*)

