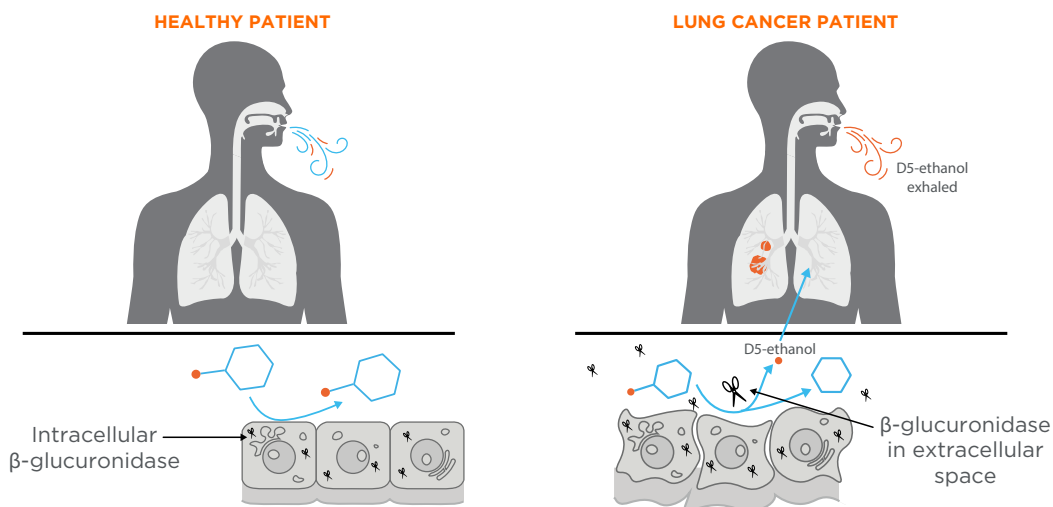


Evolution: Breath-based detection of lung cancer.

BREATH BIOPSY®

Using Exogenous Volatile Organic Compound targeting β -glucuronidase, in the tumor microenvironment.

The key issue with lung cancer is that it is typically diagnosed at later stages, reducing survival rates dramatically. This really underscores the need for early detection methods...



In the Evolution trial we are evaluating the viability of D5-ethyl- β D-glucuronide as an exogenous volatile organic compound (EVOC) probe for human lung cancers. An EVOC Probe is a molecular probe, responsive to a disease-specific metabolic pathway and results in a product that can be detected and monitored on breath.

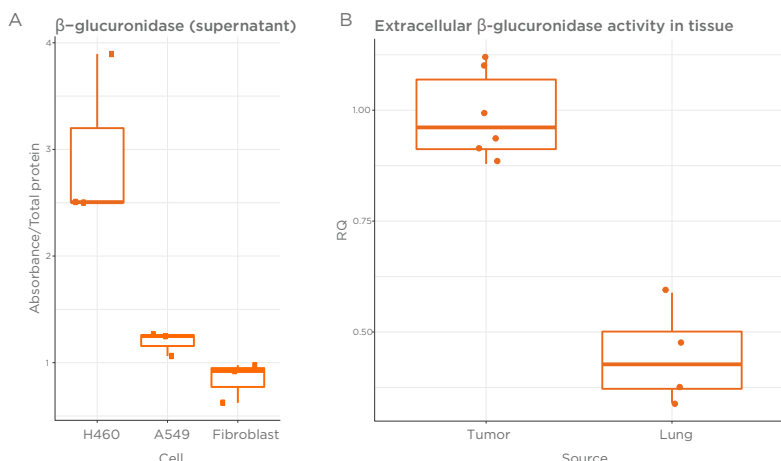
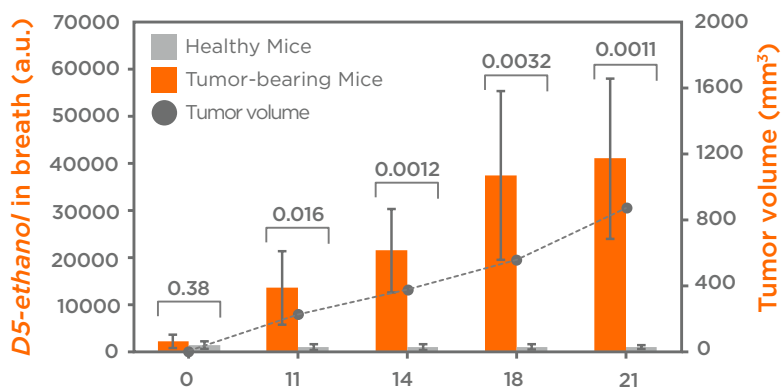
D5-ethyl- β D-glucuronide is a substrate for β -glucuronidase, a hydrolyzed enzyme that resides in the lysosome in cells in healthy tissue. D5-ethyl- β D-glucuronide is a hydrophilic compound with low cellular permeability and therefore cannot reach the β -glucuronidase in healthy tissue. In solid tumors however, β -glucuronidase is expressed in the extracellular space and is therefore accessible to the probe resulting in the release of D5-ethanol, a volatile organic compound (VOC) detectable on breath, that is not a product of normal metabolic processes in healthy individuals.

...a breath test for lung cancer represents a non-invasive preferable approach with screening that would be more affordable, easy to use, and more accessible than other existing options...

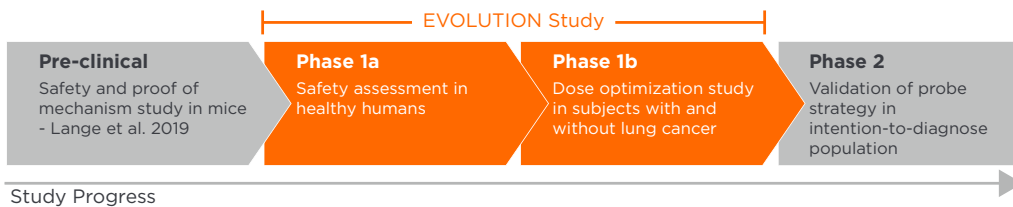
In 2019 Lange et al. published "Volatile Organic Compound Based Probe for Induced Volatolomics of Cancers" demonstrating a clear difference in D5-ethanol levels between tumor bearing mice and healthy mice with a correlation between D5-ethanol levels and tumor volume. Tumors were xenografted subcutaneously on mice and probes were administered at indicated times post tumor initiation followed by D5-ethanol measurement released from mice. Tumor volumes were measured at same timepoints.

We confirmed the extracellular activity of β -glucuronidase in lung cancer cell lines in comparison to healthy fibroblasts, and in patient derived xenograft tumor tissue compared to healthy mouse lung tissue.

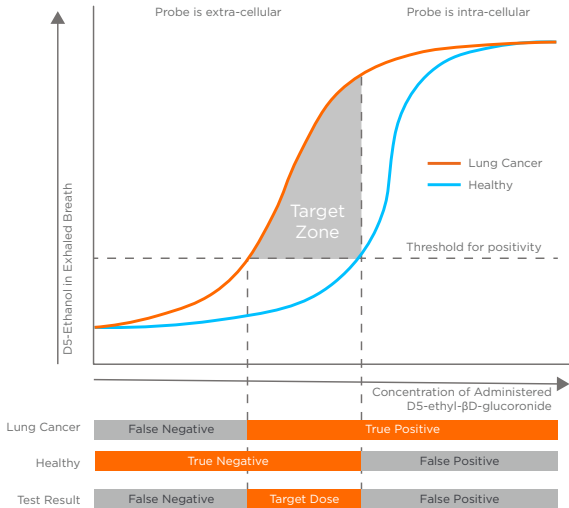
Following this we performed immunohistochemistry on both human lung cancer and healthy tissue samples, observing the expression of β -glucuronidase activity in the tumor microenvironment of all tumor pathologies at every tumor stage. No extracellular β -glucuronidase activity was detected in healthy lung tissue.



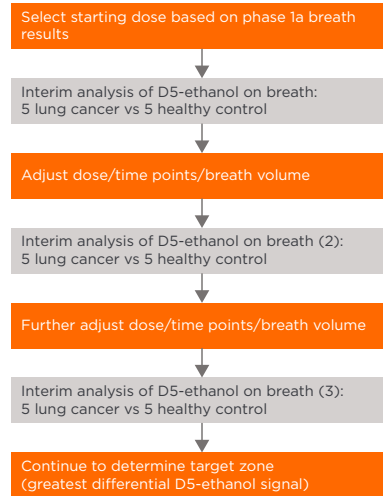
...breath is complex, and issues such as high background signal ratios and inconsistent sampling methods have so far limited progress in developing a clinically relevant breath test for cancer...



Expected dose-response curve for breath probe



Finding the target zone



Following these promising results we designed and initiated the Evolution clinical study. Phase one is divided into 1A, a safety assessment in healthy controls, and 1B, a dose optimization study in both healthy subjects, and those with lung cancer. Phase 1A was completed in 2021 with a favourable safety profile, and no concerning adverse effects. We have recently started Phase 1B where the optimal dose and timepoint for breath sampling following probe administration will be determined. Interim analysis will be carried out as data collection proceeds to determine how each of these variables need to be changed. During Phase 1B we will gather data from 50 healthy subjects and 50 subjects with lung cancer.

Find out everything there is to know about EVOC Probes:



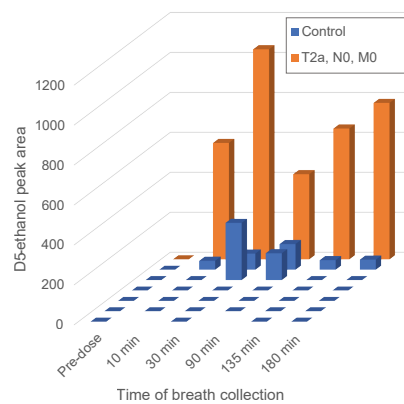
...one solution to this is the use of EVOC Probes. The administration of a molecular probe that is responsive to disease specific metabolic pathways and results in a product that can be detected and monitored on breath.

Healthy individuals and one lung cancer patient were dosed with the probe. Very low to no signal was detected in healthy individuals with a higher response in the lung cancer patient (A).

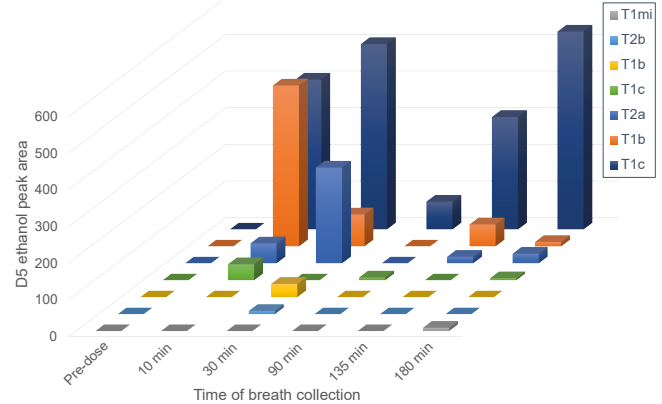
The background signal in healthy subjects was hypothesized to come from an impurity in the probe. A purer version of the probe was synthesized and administered (B).

We are excited to continue presenting the progression of the Evolution study as we gather more data.

A β-glucuronidase Probe (Impurity)



B β-glucuronidase Probe (Impurity Removed)



Contact us to find out more about collaborating with Owlstone Medical and to discuss incorporating Breath Biopsy in your cancer research.

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