

New Content  
and Functionality

Complex biologies,  
intelligently simplified.





clara<sup>T</sup> is a unique software-driven solution, classifying biologically relevant gene expression signatures into a comprehensive, easy-to-interpret report.

#### clara<sup>T</sup> benefits at a glance:

- Maximises the understanding of your dataset
- Provides readouts for the most relevant published gene expression signatures
- Standardises comparisons between different datasets
- Highlights consensus between multiple gene expression signatures
- Provides extensive supplementary data for innovative analysis

#### The opportunity created by RNA-Sequencing:

- RNA-Sequencing (RNA-Seq) is an untapped resource for biomarker discovery and development in oncology enabling the discovery and validation of an endless combination of gene expression signatures
- Gene expression signatures are more dynamic than DNA based biomarkers and better reflect changes in biology as a tumour adapts to multiple treatments
- RNA-Seq can also be used for detection of novel gene fusions and alternative transcripts





## The challenges of RNA-Sequencing:

However, there are some inherent challenges with high throughput RNA-Seq. These include:

- Complex data outputs that require advanced computational bioinformatics pipelines to develop and validate robust gene expression assays
- Analysis of multiple signatures and biologies can be time consuming, requiring significant bioinformatics / statistical resource
- There are still no PMA approved gene expression assays creating a potential regulatory risk for companies considering this approach

## clara<sup>T\*</sup> Report:

clara<sup>T</sup> is a unique reporting solution to help cancer researchers overcome the challenges associated with RNA-Seq and analysis. Samples can be sent to Almac's Labs for processing and automated generation of the clara<sup>T</sup> report.

clara<sup>T</sup> classifies publicly available gene expression signatures and single gene targets linked to multiple key biologies, alongside Almac's own proprietary assays, according to the 10 Hallmarks of Cancer. Originally published by Douglas Hanahan and Robert Weinberg in 2000. Clients are provided with a unique, interactive report that allows the easy visualisation of the key discriminating biologies within both the study cohort and an individual tumour sample.

A pan-cancer solution, based on a powerful bioinformatics pipeline, automatically generating the clara<sup>T</sup> report from raw gene expression data utilising our Next Generation Sequencing (NGS) service.

\* clara<sup>T</sup> is for research use only (RUO) and is not to be used for diagnostic or prognostic purposes, including predicting responsiveness to a particular therapy

## clara<sup>T</sup> - Utilising the Hallmarks of Cancer:

First conceptualised by Douglas Hanahan and Robert Weinberg in 2000 and subsequently updated in 2011, the **Hallmarks of Cancer** have become a paradigm within modern cancer research. The hallmarks help explain the complexity of cancer cells and describe the processes that occur allowing cancer cells to proliferate and grow if unchecked.

The clara<sup>T</sup> report utilises the Hallmarks of Cancer concept of targetable biologies to help facilitate biomarker discovery. clara<sup>T</sup> embodies the tenets set out by the authors, intelligently simplifying the complex biologies of cancer within key hallmarks.

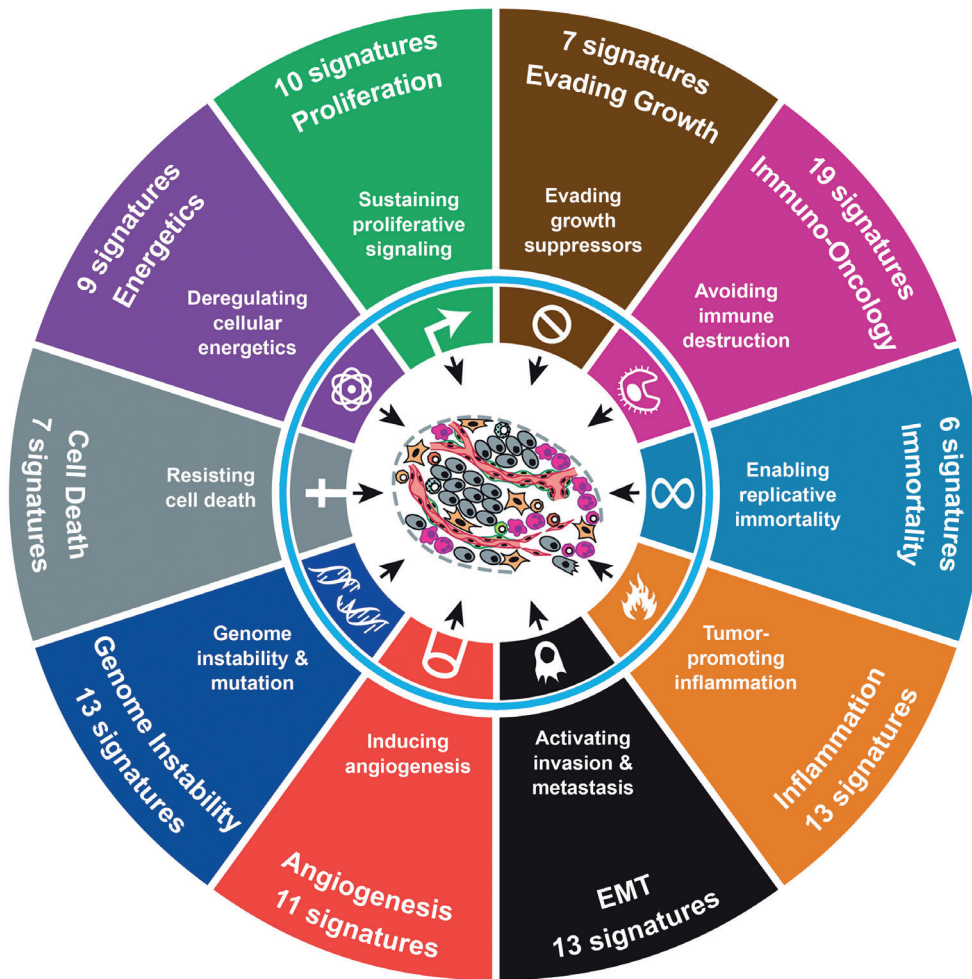


Image adapted from The Hallmarks of Cancer. Originally published in Cell 144, Hanahan D & Weinberg RA, Hallmarks of Cancer: The Next Generation, 646-674, © 2011. With permission from Elsevier.

## clara<sup>T</sup> Report - Facts:





# clara<sup>T</sup> content:



## Immuno-Oncology

### 19 signatures

- Almac I-O Assay
- 5 x TCGA Subgroups
- 2 x TILs Signatures
- 3 x Immune Resistance Signatures
- 3 x T-cell/B-cell Signatures
- 4 x TGF $\beta$
- 1 x Immune Enrichment Score



## EMT

### 13 signatures

- Almac EMT Assay
- 5 x EMT Pan-Can Signatures
- 2 x Stromal Signatures
- 1 x MAPK Activity
- 2 x Mesenchymal Subgroup
- 1 x MEK Functional
- 1 x EMT Enrichment Score



## Inflammation

### 13 signatures

- 4 x Macrophage Signatures
- 2 x NF $\kappa$ B Signatures
- 4 x Inflammatory Response Signatures
- 1 x IL1 $\beta$  Signature
- 1 x Inflammatory Response Enrichment Score
- 1 x STAT1 Signature



## Genome Instability

### 13 signatures

- Almac DNA Damage Assay
- 2 x BRCA Signatures
- 3 x DDR Signatures
- 2 x Chromosomal Instability Signatures
- 1 x HRD Signature
- 3 x MSI Signatures
- 1 x DNA Damage Enrichment Score



## Proliferation

### 10 signatures

- 2 x HER2 Signatures
- 2 x EGFR Signatures
- 2 x MAPK Activity
- 1 x KRAS Signature
- 1 x MYC Activity
- 1 x STAT3 Signature
- 1 x PI3K/AKT Enrichment Score



## Angiogenesis

### 11 signatures

- Almac Angio Assay
- 5 x Angio Subgroup
- 1 x Hypoxia Signature
- 1 x Vascular Proliferation Signature
- 2 x Angio Predictive Signatures
- 1 x Angio Enrichment Score



## Energetics

### 9 signatures

- 3 x Glycolysis Signatures
- 2 x Hypoxia Signatures
- 2 x Metabolomic Progression Signatures
- 1 x Fatty Acid Metabolism Signature
- 1 x Oxidative Phosphorylation Enrichment Score



## Evading Growth

### 7 signatures

- 2 x E2F Regulation Signatures
- 1 x Cell Cycle Signature
- 1 x CDK4 Classifier
- 1 x RB-loss Signature
- 1 x TP53 Signature
- 1 x G2M Checkpoint Enrichment Score



## Cell Death

### 7 signatures

- 2 x TNF $\alpha$  Signatures
- 1 x TP53 Signature
- 1 x TRAIL Activity
- 1 x Apoptosis Pathway Signature
- 1 x Autophagy Pathway Signature
- 1 x Apoptosis Enrichment Score



## Immortality

### 6 signatures

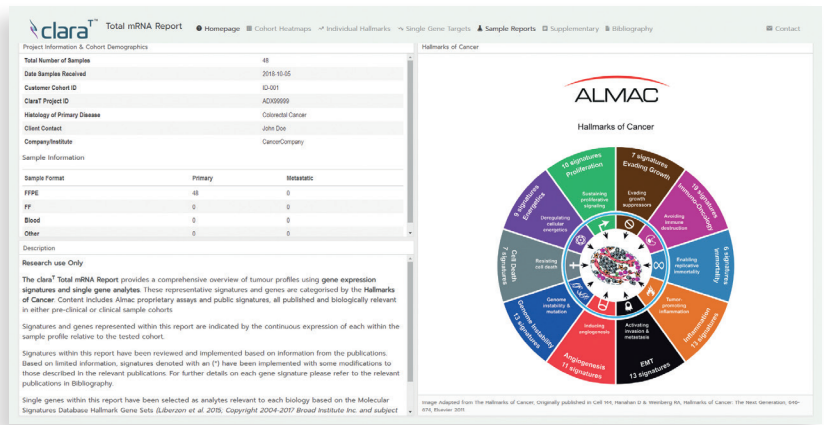
- 4 x Senescence Signatures
- 2 x Telomerase Signatures

# clara<sup>T</sup> Cohort Report:

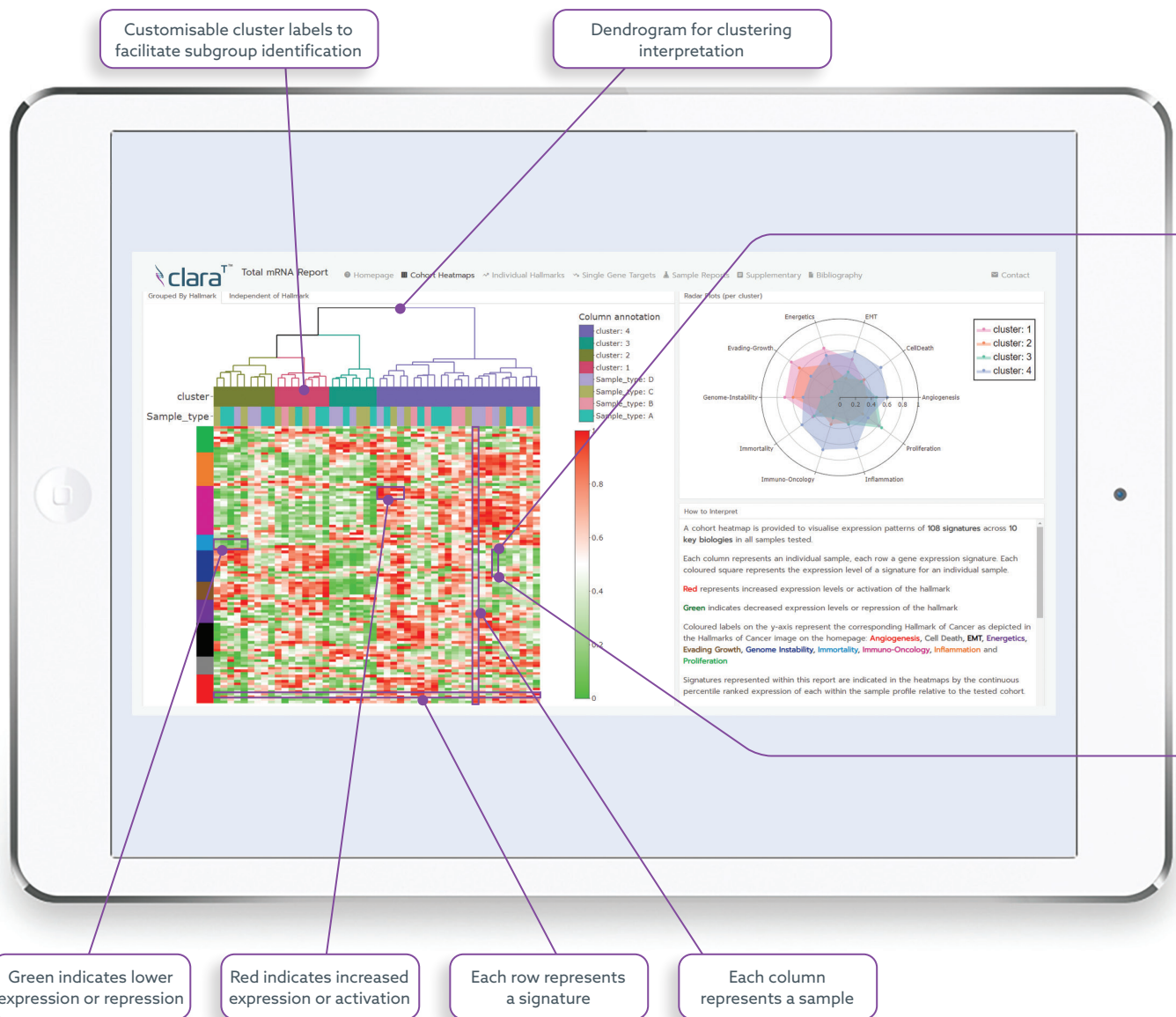
The clara<sup>T</sup> Cohort Report simplifies visualisation of expression levels across a range of the most relevant published multigene signatures allowing for quick and easy interpretation of results relating to each Hallmark of Cancer.

## Advantages of the clara<sup>T</sup> Cohort Report:

- Discover patterns of gene expression within your cohort
- Identify unique molecular subgroups within your dataset
- Determine groups of consensus gene expression signatures
- Highlight any differences or unexplained anomalies between samples



## clara<sup>T</sup> Report Homepage





## clara<sup>T</sup> Sample Report:

The clara<sup>T</sup> Sample Report gives greater insight into an individual sample and allows more detailed investigation of expression levels across signatures and single gene targets within a particular Hallmark of Cancer.

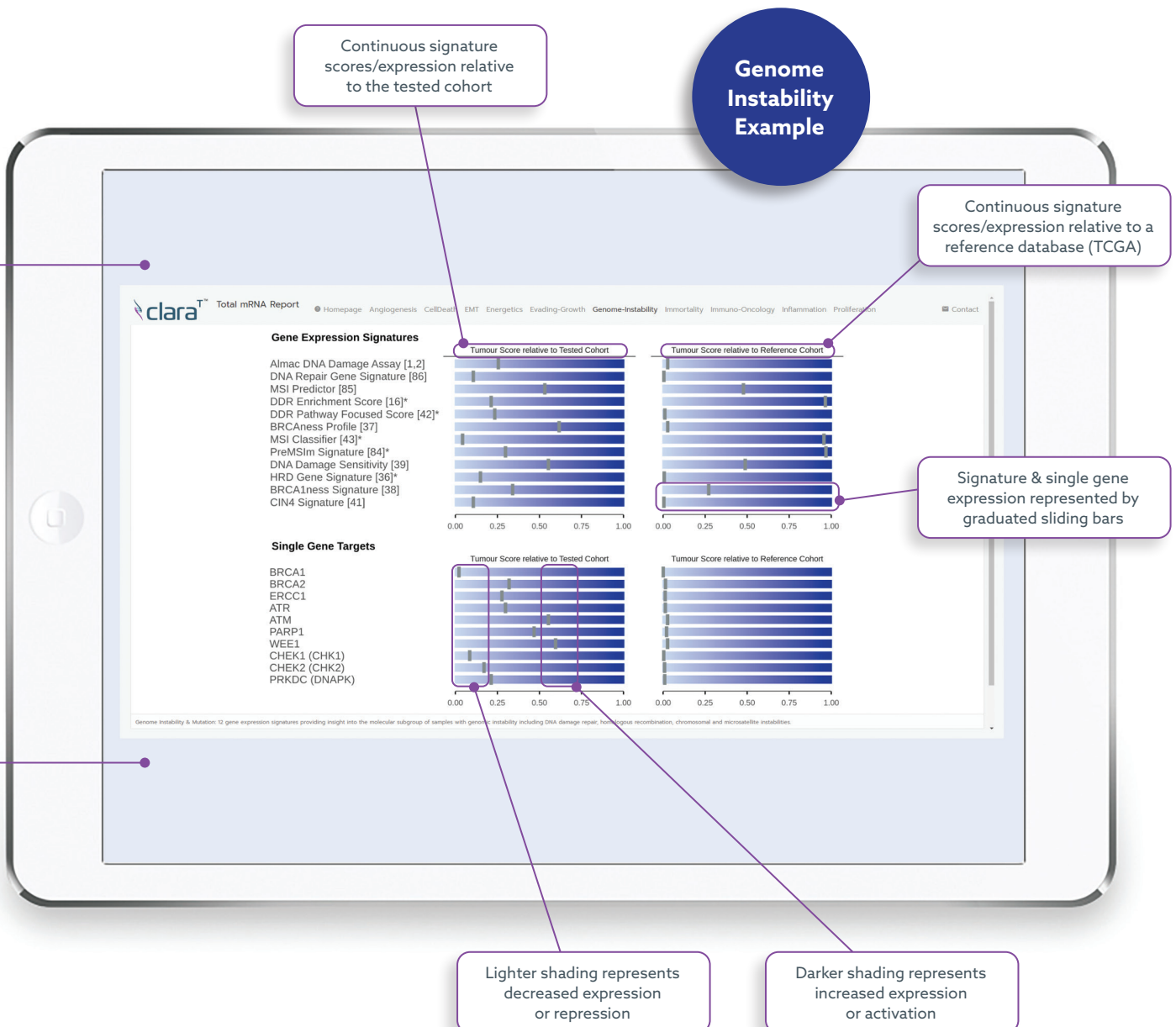
**Supplementary files** are also included in the report to support additional analysis.

### Advantages of the clara<sup>T</sup> Sample Report:

- Determine the biological profile of your sample relative to the full cohort and a reference database
- Identify the most relevant gene expression signature / biology for your sample
- Identify key pathways of activity or repression in individual samples

Signature	Signature, as named in report	Biology	S1995_00002_57_RL_001	S1995_00004_51_RL_001	S1995_00007_57_RL_001	S1995_00011_56_RL_001	S1995_00012_57_RL_001	S1995_00013_57_RL_001
1	Almac_Angio_Assay	Angiogenesis	-0.658166	-0.680336	-0.856513	-0.309258	-0.832394	
2	Anders_et_al	Global Angio Signature [33]*	39.5804	48.9645	50.3477	67.4027	45.4991	
3	Bentzen_et_al	Angiogenesis Signature B [34]*	3.38957	3.27382	3.28759	4.928471	3.593392	
4	DCosta_et_al	Angio Mixed Signatures [79]	-1.9661	-17.4682	-47.9038	-14.4453	-46.9889	
5	Franzosi_et_al	Angio/Hypoxia Signature [31]	12200.676	8553.162	8311.97	9057.806	10647.231	
6	Franzosi_et_al	Angiogenesis	15970.25	9508.29	16743.31	17983.6	16825.24	
7	Glinisky_et_al	MTS Signature [30]	-3.25793957	-6.18484531	-0.38142757	-2.07736637	0.10546648	
8	HALLMARK_ANGIOGENESIS	Angio Enrichment Score [40]*	13261.92	1850.38	12676.58	13747.97	13133.57	
9	HALLMARK_COAGULATION	Angiogenesis	10762.24	10571.65	10674.14	10769.73	11435.18	
10	HALLMARK_HYPOXIA	Angiogenesis	13089.61	13424.04	12576.52	13766.4	13252.17	

## clara<sup>T</sup> supplementary Data Files





## clara<sup>T</sup> benefits:

**Maximises the understanding of your data set** - By providing 108 individual signature outputs and multiple single targets aligned to the Hallmarks of Cancer, clara<sup>T</sup> enables you to instantly find the most important patterns from your RNA-Seq data that will inform your research going forward.

**Provides readouts for the most relevant published gene expression signatures** - Easy-to-interpret gene expression scores are displayed in the report for the most important signatures published in leading cancer journals. Providing instant information on how they perform in your dataset. Overall, this saves time identifying and implementing the most appropriate and robust gene expression signatures.

**Standardises comparisons between different datasets** - clara<sup>T</sup> is a validated and version controlled analysis pipeline providing reproducible and precise outputs in an automated fashion, ensuring data analysis is standardised across multiple cohorts, removing variation between different discovery approaches.

**Highlights consensus between multiple gene expression signatures** - The ability to simultaneously visualise multiple different gene expression signature readouts enables subtype discovery by consensus analysis resulting in greater confidence in data interpretation.

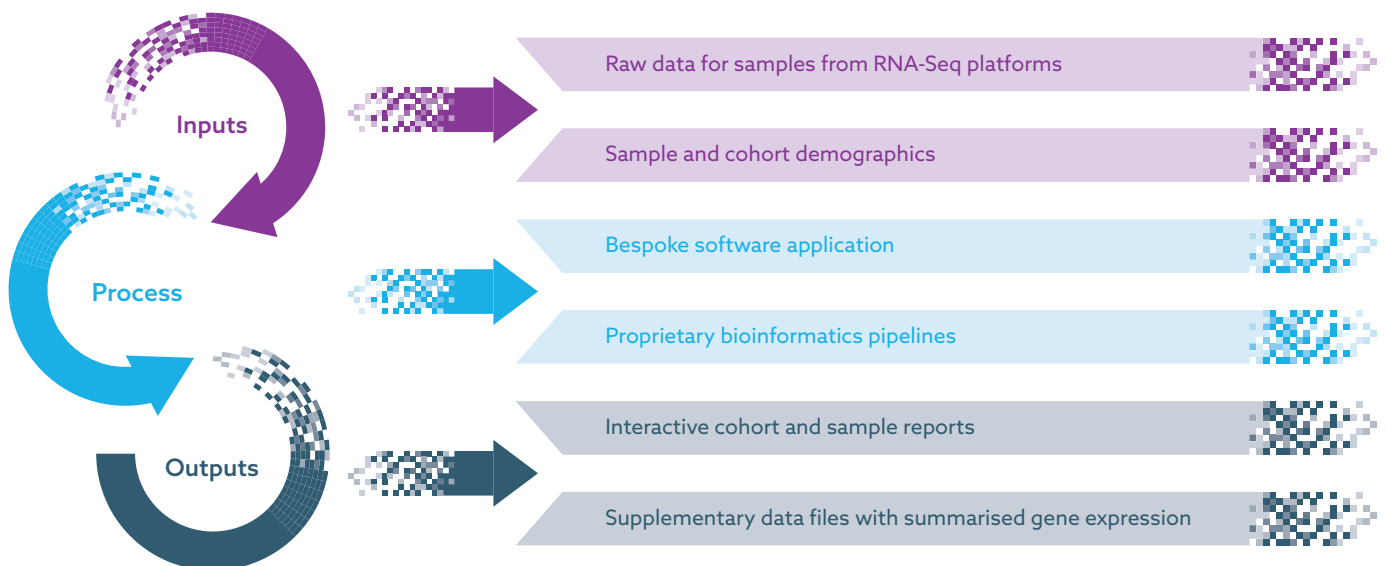
**Provides extensive supplementary data for more innovative analysis** - The supplementary data files allow researchers to spend less time on routine exploratory analysis. Allowing additional focus on novel insights through integration of signature outputs to analytics tools and clinical databases, facilitating more innovative biomarker research.





Cain Diver, Laboratory Scientist

## clara<sup>T</sup> workflow:



clara<sup>T</sup> reports can be generated from samples profiled by RNA-Sequencing at Almac labs or alternatively from gene expression data you may already have generated from your study cohort.



## How to order clara<sup>T</sup>:

**Call | Speak to a Business Development Manager | Contact us online**

- Go to the Almac Diagnostic Services' website [www.almacgroup.com/diagnostics](http://www.almacgroup.com/diagnostics)
- Click on the clara<sup>T</sup> page and fill in the contact us form
- One of our Business Development Managers will be in touch to discuss your requirements
- Almac Diagnostic Services will send a quotation based on your specific requirements
- If proceeding, complete the scope of work and sample manifest, sign the T&Cs and return to [clarasupport@almacgroup.com](mailto:clarasupport@almacgroup.com)
- A primary point of contact will be assigned to you for the duration of your project





## About Almac Diagnostic Services:

**Almac Diagnostic Services** support global pharma and biotech companies with their biomarker strategies from discovery through to companion diagnostic partnerships. Almac has clinical and research laboratories in Europe and the USA, alongside strategic partnerships in China, enabling us to support global studies. The services offered fall into three main categories:

**Genomic Services** (Range of Platforms & Technologies, Sample Management, Data Sciences).

**Clinical Trial Assays** (Research Use Assays, Clinical Use Assays, Global Clinical Trial Testing).

**Companion Diagnostics** (CDx Development, CDx Manufacture, CDx Commercialisation).

Want to know more about how clara<sup>T</sup> can help your biomarker discovery and translational research?

[almacgroup.com](http://almacgroup.com)

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