

Complex biologies,
intelligently simplified.





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

clara^T benefits at a glance:

- Maximises the understanding of your data set
- Provides readouts for the most relevant published gene expression signatures
- Classifies using the Hallmarks of Cancer for easy interpretation
- Interactive cohort and sample report
- Multiple signatures from a single tumour sample
- Cost effective solution, saving analysis time

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



Hannah Millar, Senior Laboratory Scientist

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^{T*} Report:

clara^T 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^T report.

clara^T 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^T report from raw gene expression data utilising our Next Generation Sequencing (NGS) service.

* clara^T 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^T benefits:

Maximises the understanding of your data set

- 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.

Classifies using the Hallmarks of Cancer for easy interpretation

- Gene expression signatures and single gene target outputs within the report are classified using the Hallmarks of Cancer and clustered according to their underlying biologies for simple interpretation.

Interactive cohort and sample report -

The interactive report can be reviewed online, providing an intelligent visualisation of expression patterns in all samples tested within the cohort. Additional functionality allows for further click through to all individual sample reports for more detailed investigation.

Multiple signatures from a single tumour sample

- A single sample sent to Almac for profiling, sequenced on an optimised NGS technology platform, with a powerful bioinformatics pipeline producing multiple signature readouts. Saving precious tissue samples, time and cost.

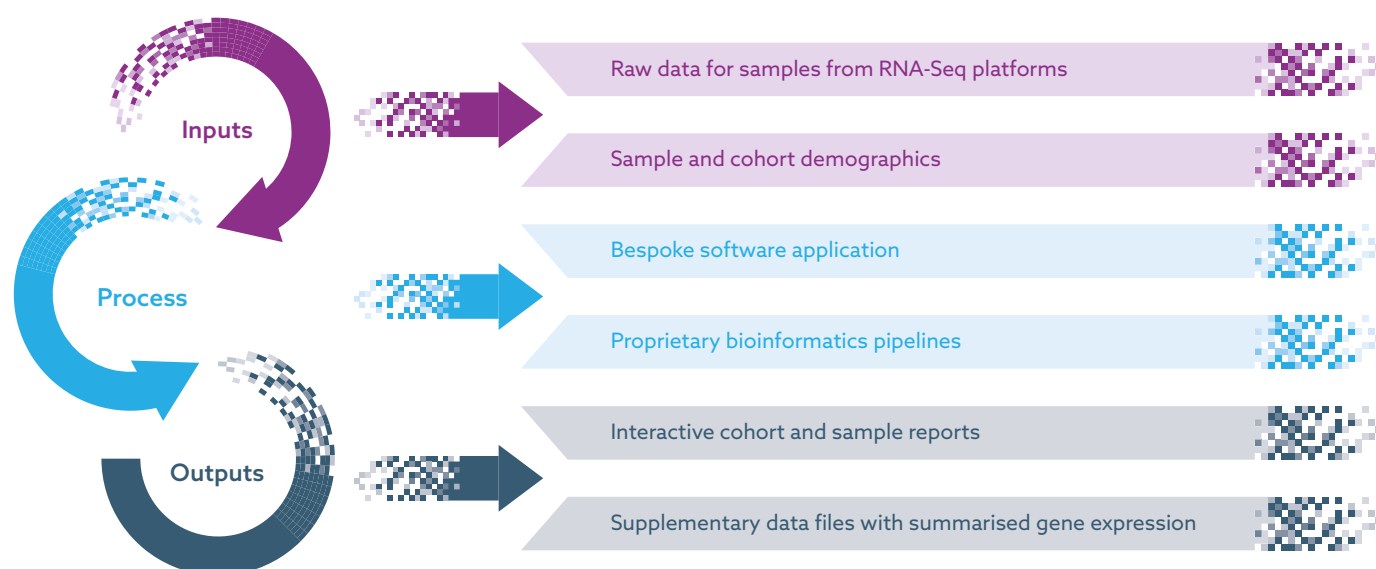
Cost effective solution, saving analysis time

- Cancer researchers can benefit from detailed, actionable analysis of RNA-Seq data from the report without investing in additional significant time and resource to perform in-house bioinformatics analysis.



Cain Diver, Laboratory Scientist

clara^T workflow:



clara^T Cohort Report:

The clara^T Cohort Report and interactive heat map simplifies visualisation of expression levels across a range of the most relevant published multigene signatures allowing for quick and easy interpretation of results.

The signatures are classified across the Hallmarks of Cancer.

Advantages of the clara^T Cohort Report:

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

Research Use Only

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Fax: +65 (0) 20 352 8375
info@almacdiagnostics.com

Client Information & Cohort Demographics

Customer Cohort ID: _____

clara^T Project ID: ADX _____

Total No. of Samples: _____

Date Samples Received: (DD/MM/YYYY)
e.g. 01/01/2018

Histology of Primary Disease: _____

Site of Collection: Primary ☐ Metastatic ☐
Tick as appropriate

No. of Samples: _____

Sample Format: FFPE ☐ FF ☐ Blood ☐ Cell Lines ☐
Tick as appropriate

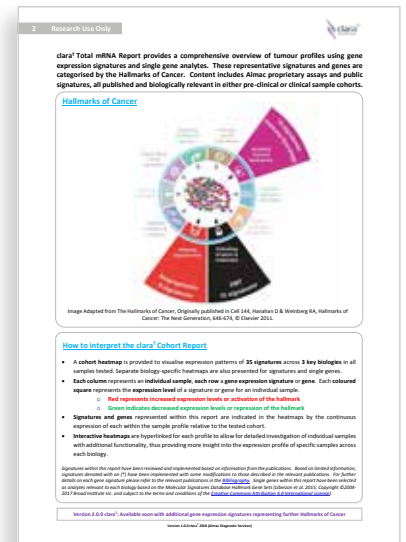
Client Contact: _____

Company/Institute: _____

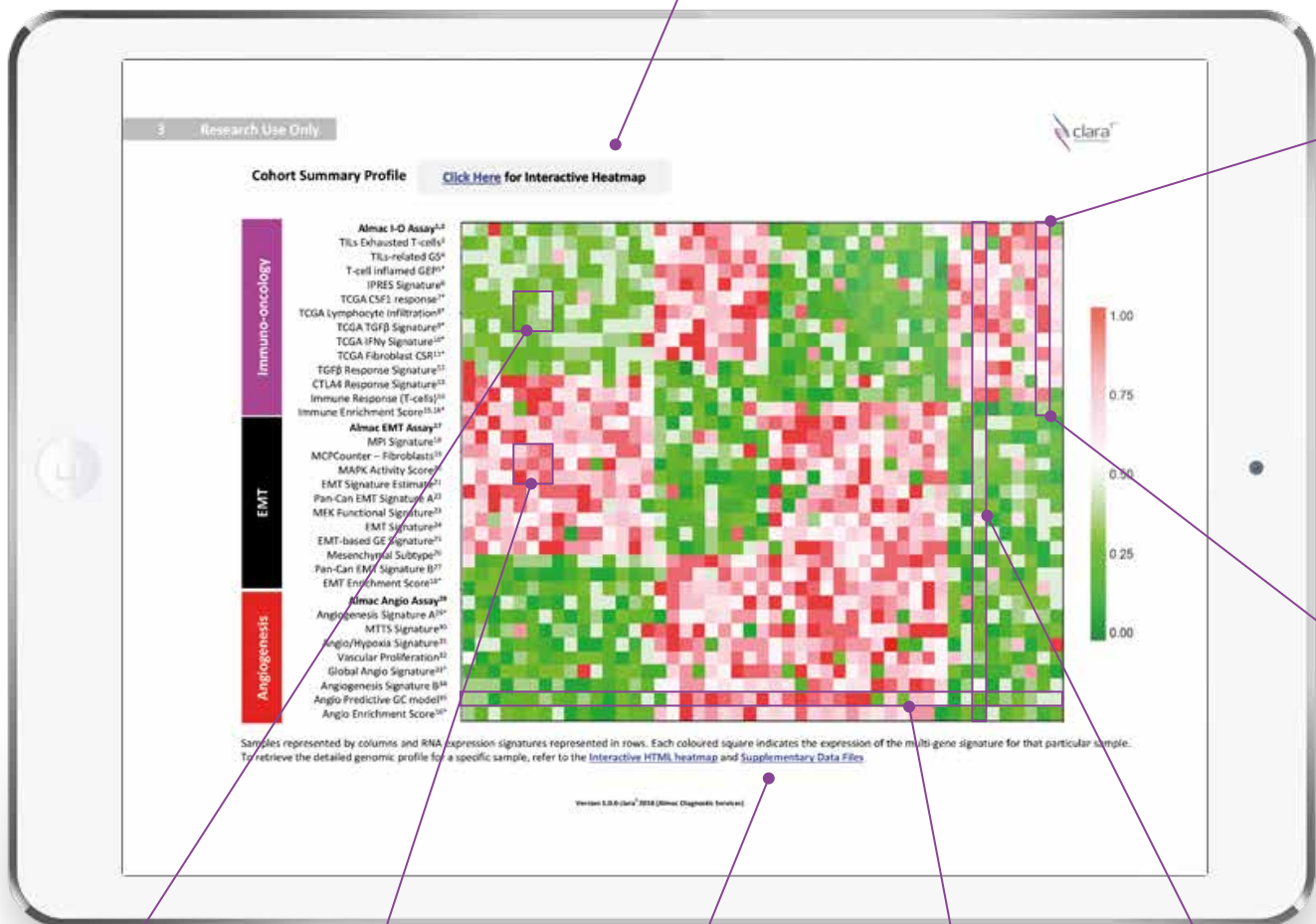
Customer Support: If you require any further information on ordering please contact: Almac Diagnostic Services (ADS) Customer Support at +65 (0) 20 352 7575 (9:00-17:00 SGT), 7 days per week or sales@almacdiagnostics.com

Research Use Only: This information provided within this report should not be used for diagnostic or prognostic purposes, including predicting responsiveness to a particular therapy.

Version 3.0.0 (clara^T ADS (Almac Diagnostic Services))



Includes an interactive heat map



Green indicates lower expression or repression

Red indicates increased expression or activation

Includes supplementary files with summarised scores for all signatures

Each row represents a signature

Each column represents a sample

clara^T Sample Report:

The clara^T 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.

Interactive supplementary files are also included in the report and are hyperlinked within each profile for additional data functionality.

Advantages of the clara^T Sample Report:

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

Research Use Only

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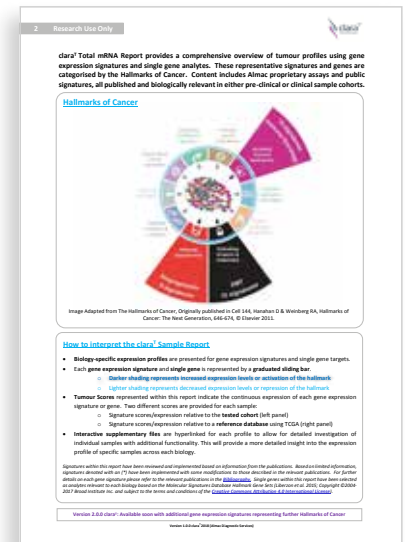
Client Information & Sample Demographics

clara^T Project ID: _____ ADX: _____
Customer Sample ID: _____
Almac Sample ID: _____
Histology of Primary Disease: _____
Country of Origin: _____
Patient Age: _____
Gender: Male ☐ Female ☐
Tick as appropriate
Site of Collection: Primary ☐ Metastatic ☐
Tick as appropriate
If Metastatic please provide site:
Sample Format: FFPE ☐ FF ☐ Blood ☐ Cell Lines ☐
Tick as appropriate
Client Contact: _____
Company/Institute: _____

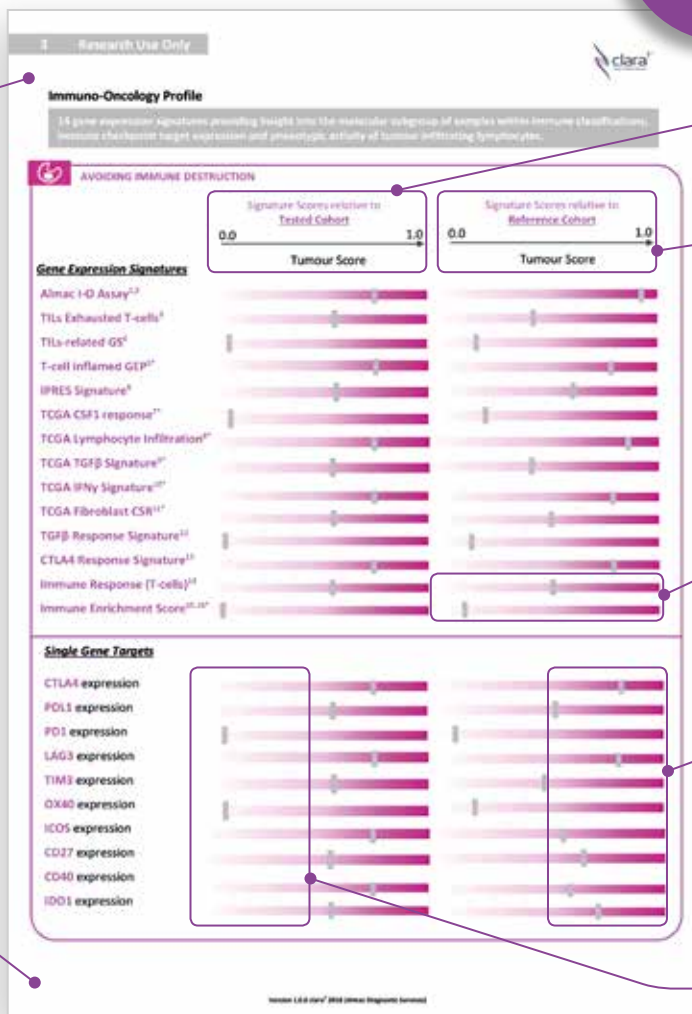
Customer Support: If you require any further information or assistance please contact: Almac Diagnostic Services clara^T Customer Support at clara@almacdiagnostics.com or 01223 303 7575 (UK only). Your use of clara^T is subject to the [Almac Diagnostic Services clara^T Terms and Conditions](http://www.almacdiagnostics.com/terms).

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Version 1.0.0 clara^T (Almac Diagnostic Services)



Immuno-Oncology Example



Continuous signature scores/expressions relative to the tested cohort

Continuous signature scores/expressions relative to a reference database (TCGA)

Signature & single gene expression represented by graduated sliding bars

Darker shading represents increased expression or activation

Lighter shading represents decreased expression or repression

Hallmarks of Cancer:



clara^T Initial Hallmarks Covered:

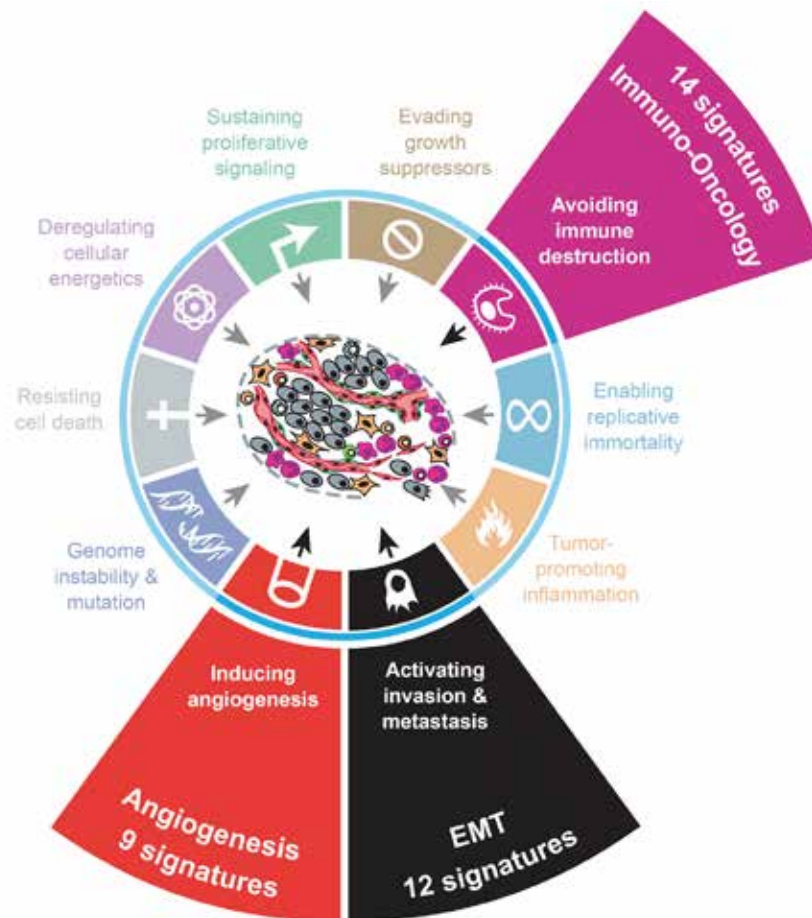


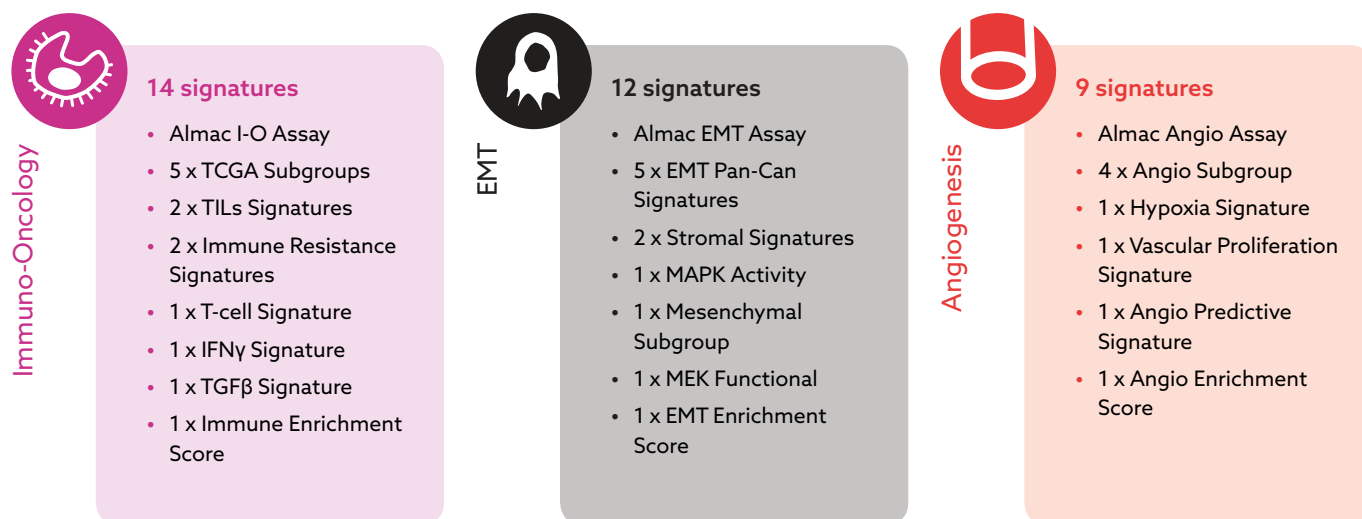
Image adapted from The Hallmarks of Cancer. Originally published in Cell 144, Hanahan D & Weinberg RA, Hallmarks of Cancer: The Next Generation, 646-674, © 2011. With permission from Elsevier.

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

clara^T launch content:



For further details on these signatures refer to the clara^T Fact Sheet.

Initial clara^T Report – Facts:

- **3 key biologies**
- **35** gene expression signatures
- **30** drug targets
- **1,641 single genes** relevant to launch content

clara^T Future Report:

Almac will continue to expand the clara^T report by developing content to eventually cover **all 10 Hallmarks of Cancer**.



How to order clara^T:

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

- Go to the Almac Diagnostic Services **website**
www.almacgroup.com/diagnostics
- Click on the clara^T 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 claratsupport@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 is a global stratified medicine company specialising in biomarker driven clinical trials, with laboratories in the UK, USA and a partner laboratory based in China.

As part of the wider Almac Group, we are a stable, privately owned business that is growing globally in line with increased customer demand. Our diagnostic experience spans oncology, immunology, CNS and infective diseases.

Want to know more about how clara^T can help your biomarker discovery and translational research?

almacgroup.com

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