Tumour plasticity

Topic details

Action type	Research and Innovation Action (RIA)
Submission and evaluation process	2 stages
IMI2 JU Strategic Research Agenda - Axis of Research	Innovative medicines
IMI2 JU Strategic Research Agenda - Health Priority	Cancer

Specific challenges to be addressed by public-private collaborative research

The last decade has seen tremendous advances in the development of effective targeted therapies as well as in immuno-oncology to more effectively treat cancer. Despite this, cures are still rare in the metastatic setting. In most cases, an initial response to treatment is followed by the eventual emergence of **drug resistance** [1]. Drug resistance in cancer is one of the greatest causes of mortality, and despite increasing success with targeted therapies in the clinic (including immunotherapy), the mechanisms by which cancer cells evade cell death are still not well understood. Drug combinations are likely to be critical to overcoming drug resistance but are dependent on identifying the cellular programmes that cancer cells use to resist therapeutic agents.

In tumours that initially respond to treatment, rare cancer cells can survive and withstand therapy **('drug tolerant persister' cells, DTPs**) and can act as a reservoir for the eventual emergence of drug resistance (**Figure 1**) [2]. Furthermore, these studies have shown that these cells are able to survive drug treatment by altering the transcriptional state of specific signalling pathways, and that in the early stages such changes are plastic and reversible, but that over time these changes become stable and fixed.

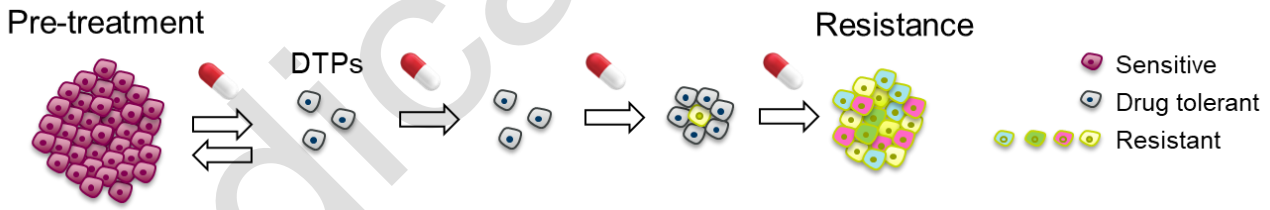

Figure 1. Diagram showing how drug tolerant persister cells (DTPs) arise from the bulk tumour following successful treatment, and ultimately contribute to the emergence of drug resistance.

Recent technological advances in **single-cell sequencing** have revolutionised the study of individual cells within cancer populations and, importantly, would allow the characterisation of DTPs, something previously impossible with bulk sequencing technologies [3]. Single-cell sequencing provides information that is not confounded by genotypic or phenotypic heterogeneity of bulk samples. Importantly, it has confirmed the existence of DTPs in patients following treatment response and, more importantly, the characterisation of the transcriptionally altered pathways in DTPs [2][4]. Characterising the transcriptionally altered pathways in persister cells, the biological processes they regulate and their druggability will be critical to **future drug combination strategies**, with the goal of preventing or significantly delaying the development of drug resistance.

There are numerous challenges in applying single cell sequencing to drug resistance- arguably one of the most important barriers to curing cancer today, and specifically:

- defining best sequencing protocols – single-cell RNA-sequencing (scRNA-seq) is a fast-moving field with a recent benchmarking paper comparing 13 different methods [5];
- computational approaches to big data – as with sequencing methods, the analysis framework is constantly evolving and there are challenges in integrating data across studies and platforms;
- standardisation of data formats;
- best practice single cell collection from *in vitro* and *in vivo* model systems;
- application of single-cell sequencing to clinical samples;
- spatial imaging technologies;
- biological interpretation of data, including novel target identification.

This topic proposes to apply state-of-the-art single-cell sequencing technologies to characterise cancer cell populations pre-treatment, at minimal residual disease (for DTPs), and upon the acquisition of drug resistance and from a variety of pre-clinical human and mouse models as well as clinical samples.

Scientific advances in singe-cell sequencing, use of patient-derived xenografts (PDX) and patient-derived organoids (PDO), and clinical tissue imaging have come together to create the perfect environment to address one of the most important challenges in cancer biology today: **drug resistance**. Each of these areas is a rapidly advancing field and, importantly, no single sector has complete expertise in all these areas. Additionally, the collection and sorting of cells in a standardised way is well-aligned with the capabilities of industry partners and is an activity that academic groups are typically not well set up to deliver at scale. Conversely, the techniques for evaluating single cells and the computational methods for interpretation of data are under constant development (mainly in academic labs). Finally, industry partners are ideally placed to interrogate different drug mechanisms against common tumour backgrounds (or vice versa). Taken together, these factors provide a compelling opportunity for private-public collaboration.

Therefore, to address such a wide range of complex issues, there is a need for strong cooperation amongst industry, biotechnology companies, academia, and patient organisations, bringing their diverse expertise in the following fields:

- acquisition of single-cells from pre-clinical and clinical models;
- adoption of best single-cell sequencing practice;
- standardisation of analytical methods, including data integration across studies;
- application of scRNA-seq to characterise non-malignant cells in the tumour microenvironment;
- spatial transcriptomics and imaging techniques;
- development of protocols for clinical single-cell sequencing.

This Call topic is an ideal opportunity to systematically address how viewing a patient's cancer not as a single homogeneous entity but rather as a population (containing diverse subpopulations with different behaviours) might ultimately alter the paradigm of drug resistance.

The strategic relationship between leading scientists and key opinion leaders in industry, small and medium-sized enterprises (SMEs) and academia will enable a better understanding of drug development post-novel

target identification, and increase the likelihood of spin-off projects based on the better understanding of DTP biology.

Scope

The overall objective of the Call topic is to use state-of-the-art single-cell sequencing to understand and overcome drug resistance in cancer by **characterising the biology of drug tolerant persister cells**, building the capability for such studies across Europe.

The call topic will address primarily adult tumours, with the provision to include childhood tumours where appropriate models are available at a later stage of the programme. To optimise our ability to determine the role of tissue lineage on the biological processes observed in single-cells, we propose that the majority (>80 %) of the single cells should be provided from drug treatments in 3 adult cancers:

- non-small cell lung cancer (NSCLC);
- breast cancer;
- colorectal cancer.

Each industry partner will nominate five tumour types/drug treatments aligned to the tumour areas summarised above and it is expected that nomination of study systems will be in consultation with academic consortium partners. Upwards of 20 % of the studies can be proposed in tumour types in addition to these 3 core cancers, including childhood cancers.

We anticipate that most of the single cells from the models described above will be provided by the industry partners, while the academic consortium will provide expertise in single-cell sequencing and data analysis.

To facilitate data integration across studies, it is preferable to use a small number of sequencing technologies that are complementary, well supported and widely used, and which are able to analyse large numbers of single cells versus smaller number of cells at greater depth of coverage. For these reasons, the Chromium (10X Genomics) [6]and Smart-Seq2 [7] platforms are preferred as the main complementary single-cell sequencing technologies used for the implementation of the proposed activities. These are mature, commonly used protocols that have been extensively benchmarked.

The goals of the Call topic are:

- To characterise the biology of Drug Tolerant Persister cells - defining the signalling pathways and cellular processes that enable DTPs to survive drug treatment and thereby identify novel drug targets to overcome this – using state-of-the-art single-cell sequencing and spatial transcriptomics in a range of cancer models.
- To better understand the tumour microenvironment – to avoid solely focusing on cell intrinsic drug resistance programmes, a key element of the work packages should be to use spatial imaging techniques to explore the interaction between cancer cells and the microenvironment.
- Generation of single cell RNAseq data from adult and childhood cancers – although the pre-clinical models used to explore the biology of drug treatment in cancer are predominantly based on adult cancers, drug resistance is equally a major problem in childhood tumours. The applicants should anticipate that from year 3 of the funded project, specific childhood cancers (up to 20 % of the total studies proposed) could be considered for inclusion where the appropriate models are accessible and where there is a hypothesis relationship with drugs or tumours being investigated by the consortium. To develop best practice in clinical validation and single-cell sequencing – clinical validation will be key to translation of any findings and a change in clinical practice. To include informed patient consent forms that cover all intended uses, including clinical outcome data and sharing of data inside the consortium and with 3rd

parties. General Data Protection Regulation (GDPR) compliant tracking of patient data, samples and PDXs.

- To create gold standard protocols for single cell collection – across a range of models and to include differing methods for isolating single cells from human (organoids, clinical biopsies) and mouse (PDX, genetically engineered mouse models (GEMM) and syngeneic mice) model systems.

- To develop core analytical methods – use pre-treatment, on treatment and post-treatment single-cell sequencing data to develop novel computational approaches to identify the different subtypes of cancer cells present, and the biological processes that are complicit in maintaining their survival following drug treatment.

- To build EU capability in single-cell sequencing – in the process of developing the protocols for single cell collection, sequencing and analysis, the funded project will put in place infrastructure to enable other groups in the EU to carry out similar single-cell sequencing studies in both cancer and non-cancer models.

Importantly, despite the fact that over the five years of the funded project we expect to adopt new technologies as and when they are developed and where they demonstrate significant advantages over current protocols, the goal of this Call topic is not the explicit development of such new methods and technologies *per se*. Additionally, we do not expect all of the drug-tumour combinations for study to be fixed at the outset. This will emerge as the industry partners identify agents and systems for study and will be managed by a consortium portfolio review process.

Expected key deliverables

The expected key deliverables should include the following:

Deliverable 1: Benchmarked and standardised protocols for single cell identification and collection from PDX/PDO models.

Deliverable 2: Gold standard methods for tissue-based spatial imaging. To include pre-clinical models as well as clinical samples for validation in relevant patient populations.

Deliverable 3: Multi-omics methods for characterising single cells. Incorporate new technologies such as CITE-seq (single-cell RNA sequencing and cell surface antibody expression), combined ATAC-seq/scRNA-seq and single-cell metabolomics protocols.

Deliverable 4: DTPs and metadata/annotation from human and mouse models. Provision of single cells from various time points (pre-treatment, on treatment and tumour progression) in (typically) 3-6 models per cancer type, and including pre-clinical (PDO, PDX, GEMM and syngeneic models) and clinical samples. Additional models from non-industry partners will also be permitted.

Deliverable 5: State-of-the-art analysis methods of single-cell sequencing. Define regulatory networks from transcriptional data as well as druggability of relevant targets and identify novel drug combinations to prevent the emergence of DTPs following treatment in the relevant cancers.

Deliverable 6: Single-cell measurement data combined with treatment and outcome data / clinical outcome data.

Deliverable 7: Gold standard methods for the validation of key transcriptional changes. To validate transcript(s) implicated in DTP biology using spatial imaging techniques applied to treated patient samples and combining CRISPR screens with scRNA-sequencing.

Deliverable 8: Tools to allow cross-study analyses of single-sequencing data. Develop novel methods and software packages to combine data across multiple studies for enhanced power and to detect novel biology not otherwise revealed by single study analyses.

Deliverable 9: **A raw data repository with access for all consortium partners.** A repository for data (measurement raw data, preclinical treatment and outcome data and clinical treatment and outcome data) with granular access rights that supports quality control and data queries in line with access and intellectual property (IP) rights according to the IMI2 JU Grant Agreement rules and as specified in the consortium agreement. The proposal should outline how sustainability of data access will be ensured. Where patient data is generated or used, this will be integrated across studies in a legally and ethically compliant way, including any GDPR requirements.

Deliverable 10: White paper on single-cell sequencing to characterise DTP biology.

Expected impact

A comprehensive effort to prevent drug resistance in cancer is generally lacking at the present time. This topic proposes the use of state-of-the-art single-cell sequencing technologies to address this challenge across a number of the most prevalent cancer types, in both adult and childhood cancers.

A comprehensive database, profiling DTPs across a range of cancers and therapies would enable a deeper understanding of the biology of DTPs and allow cross-tumour studies.

Impact for patients:

- identification of novel drug targets in DTPs and resulting drug combinations that delay or prevent the emergence of drug resistance in cancer;
- better understanding of the contribution of tumour heterogeneity and plasticity to disease outcome, progression and relapse.

Impact for academia and SMEs:

- harmonisation of protocols for single cell experiments;
- enhanced infrastructure in the EU for single cell sequencing;
- development of gold standards for the analysis of single-cell sequencing data;
- access to comparative data on different pre-clinical and clinical models and better understanding of the biology of DTPs in cancer with a high likelihood of spin-off projects;
- improvements in single cell sequencing and spatial imaging with potential for commercial development;
- better understanding of drug development post-novel target identification.

Impact for industry:

- access to a data source for further functional studies (e.g. knock-out, knock-in, target perturbation) that will lead to opportunities for identification of novel targets in the DTP space - pointing to new targets or rational drug combinations that alter the drug resistance paradigm;
- access to single cell measurement data combined with outcome data (models) and clinical outcome data;
- development of expertise in the analysis of single-cell sequencing data;
- gold standard methods for the delivery of single cell projects.

In their proposals, applicants should outline how the project plans to leverage the public-private partnership model to maximise impacts on innovation, research & development; regulatory, clinical and healthcare practices, as relevant.

In addition, applicants should describe how the project will impact the competitiveness and growth of companies including SMEs.

In their proposals, applicants should outline how the project will:

- manage research data including use of data standards[1];
- disseminate, exploit, and sustain the project results; this may involve engaging with suitable biological and medical sciences research infrastructures[2];
- communicate the project activities to relevant target audiences.

In addition, the following additional exploitation[3]/dissemination[4] obligations must be considered to maximise impact:

- Quality control (QC), standardisation data and the agreed standardised operating procedures will be made publicly available as soon as possible;
- A mechanism needs to be proposed to ensure that input data and results generated by an industry partner working together with an academic partner are kept confidential until the dataset and experiment is complete. A process for release to the rest of the consortium will also be agreed;
- A mechanism needs to be proposed to enable third party access to results at the end of the action. A plan for aspects related to sustainability should be proposed, especially ensuring that the database remains accessible and facilitating its population with additional clinical outcome data. This can include a proposal for options transferring the open access database into an existing structure and should include realistic ideas for long-term financial and operational sustainability of the database;
- Any publications arising from the action need to link to an open access area of the consortium database to coincide with publication.

Potential synergies with existing consortia

Synergies and complementarities should be considered with relevant national, European and non-European initiatives (including suitable biological and medical sciences research infrastructures**Error! Bookmark not defined.**) in order to incorporate past achievements, available data and lessons learnt where possible, thus avoiding unnecessary overlap, and duplication of efforts and funding.

Key synergies with existing consortia that could be considered are:

- International programmes using single-cell sequencing to create reference maps of human cells (e.g. Cell Atlas programmes). In particular, dialogue with pre-existing working groups to develop standards in the generation and analysis of single-cell sequence data will be advantageous;

[1] Guidance on data management is available at http://ec.europa.eu/research/participants/docs/h2020-funding-guide/cross-cutting-issues/open-access-data-management/data-management_en.htm

[2] http://www.corbel-project.eu/about-corbel/research-infrastructures.html

[3] Article 28.1 (Additional exploitation obligations) of the IMI2 Grant Agreement will apply

[4] Article 29.1 (Additional dissemination obligations) of the IMI2 Grant Agreement will apply

- Programmes that allow the inclusion of specific pre-clinical models would add value. Programmes directed towards developing an expanded range of adult and childhood cancer PDX models are particularly relevant;

- If aligned with the goals of the Call topic, programmes already collecting clinical samples for single-cell sequencing would be valuable as some of this data could be considered for integration.

Industry consortium

The industry consortium is composed of the following EFPIA partners:

- AstraZeneca (lead)
- Bayer
- Eli Lilly
- Transgene SA
- Merck KG
- Charles River

The industry consortium anticipates contributing the following expertise and assets:

- work package co-leadership;
- contribution to database / IT solutions and bioinformatic analyses;
- contribution to samples, metadata and curation and models.

In particular, industry partners will **contribute single cell samples from the relevant human and mouse tumour models** and therapies as well as access to the relevant clinical samples. It is anticipated that nearly all of these will be in-kind, rather than background contributions. (In-kind samples will be the results of studies specifically designed for this programme and carried out during in the frame and duration of the project; if background contributions are introduced, they could include validation sets of cells collected prior to this action commencing).

During the funded action, members of the industry consortium plan to contribute scientifically relevant activities for generating data on single cells or collecting and sorting single cells in prospective activities that are part of broader industry clinical studies. The relevant activities will be included in the project's Description of the Action and are necessary for achieving its objectives. The introduction of the data constitutes an in-kind contribution which entails access rights to these project results in line with IMI2 JU IP rules. The single-cell samples will be collected from drug treatment studies in pre-clinical mouse or human tumour models (PDO, GEMM or PDX samples). The industry partners will provide samples corresponding to approximately 80 drug/tumour combinations in total. Each study will aim to collect cells at three time points. A small proportion (<20 %) of study samples will be provided for spatial and multi-omic analysis. Submitting these samples to scRNAseq analysis is an essential activity of the project and the data derived will drive better understanding of the origin of DTPs.

Optionally, prospective data will be provided by industry partners, derived from scRNAseq analysis of PDO or PDX samples and subjected to the same bioinformatic analysis as above.

In addition to project leadership, industry partners' staff efforts are expected to be largely spent on work packages 1-4 and 7 (please refer to the suggested architecture).

Indicative duration of the action

The indicative duration of the action is 60 months.

This duration is indicative only. At stage 2, the consortium selected at stage 1 and the predefined industry consortium may jointly agree on a different duration when submitting the stage 2 proposal.

Indicative budget

The financial contribution from IMI2 JU is a maximum of EUR 7 058 000.

The indicative in-kind contribution from EFPIA partners is EUR 8 500 000.

Due to the global nature of the participating industry partners, it is anticipated that some elements of the contributions will be non-EU/H2020 Associated Countries in-kind contributions.

Expertise and resources expected from applicants at stage 1

The stage 1 applicant consortium is expected, in the submitted short proposal, to address all the objectives and key deliverables of the topic, taking into account the expected contribution from the industry consortium which will join at stage 2 to form the full consortium.

The stage 1 submitted short proposals should include suggestions for creating a full proposal architecture which could be in line with the suggested architecture described below, though this architecture is only a suggestion.

This may require mobilising, as appropriate the following expertise:

Relevant technology companies, in particular SMEs, along with academic centres that have expertise in single-cell sequencing and analysis of sequencing data, as well as spatial transcriptomics, should be part of the successful consortium.

The size and budget allocation of the applicant consortia should reflect the expertise needed to achieve the proposed objectives within the indicated budget while ensuring the 'manageability' of the consortium as well as efficient and effective teamwork. Therefore, the number of members of the applicant consortium needs to be thoroughly justified in the proposal and all partners involved should make a significant contribution to the proposed work.

Specifically, the applicant consortium should be able to demonstrate (through publications, consortia leadership, local capability development, grants):

- the technical expertise to carry out single-cell sequencing using technology platforms that are mature, well-supported and widely used, as well as technical expertise in spatial transcriptomics techniques;
- expertise in the development of new versions of single cell technology, plus a demonstrated ability to evaluate and rapidly internalise new single cell techniques;
- expertise in parallel single-cell sequencing technologies that capture epigenome-transcriptome interactions e.g. scNMT-seq (chromatin accessibility, methylation and transcription sequencing) [8];
- expertise in the bioinformatics analysis of single-cell sequencing data, spatial transcriptomics, gene regulatory network reconstruction, and computational approaches to novel target identification;
- expertise in the data integration of single-cell RNA-seq datasets across multiple platforms, individuals, and centres [9];

- to support standardisation of data, adherence to the FAIR principles ('findable, accessible, interoperable and reusable') [10];

- where there is a proposal for the applicant consortium to provide single-cells for sequencing, it should demonstrate the ability to deliver single cells from the relevant human (clinical, PDO) and mouse (PDX, GEMM, syngeneic) tumour models and from pre-treatment and treated models, with fixation/storage as specified in the consortium SOPs. Applicants should demonstrate the feasibility of collecting the outlined number of samples based on selected cancer types/therapies (see Deliverables);

- ability to coordinate a large research initiative and to create a scientific network.

The applicant consortium is expected to set up a governance structure that includes the necessary project management skills suitable for the consortium and activities. This could be ensured by one of the publicly funded partners, who in this case would need to have significant project management and coordination skills as well as the necessary experience in supporting complex – per size and composition – consortia in IMI/EU funded projects.

Considerations for the outline of project work plan

In their stage 1 proposals applicants should:

- Give due visibility to data management; dissemination, exploitation and sustainability; and communication activities. This should include the allocation of sufficient resources for these tasks which will be further developed in the stage 2 proposal;

- Consider including a strategy for ensuring the translation of the project results to drug development, regulatory/ health technology assessment (HTA) settings (e.g. through scientific advice/ qualification advice /opinion, etc.), clinical and healthcare practices and/or decision-making processes.

Suggested architecture

The public partners are expected to carry out most of the sequencing work whereas industry partners contribute in kind in the form of single cells (collected specifically for this programme) so that work can be carried out centrally with clear streamlined processes. Both industry and public partners will collaborate in the analysis of the data. Steering of the individual work packages and content decisions will be done jointly by the public and private partners.

For clarity, there will also be an opportunity for non-industry consortium partners to provide samples from up to 20 drug/tumour combinations, assuming that the models are appropriate with a hypothesis relationship with drugs or tumours being investigated by the consortium as agreed by the portfolio management process.

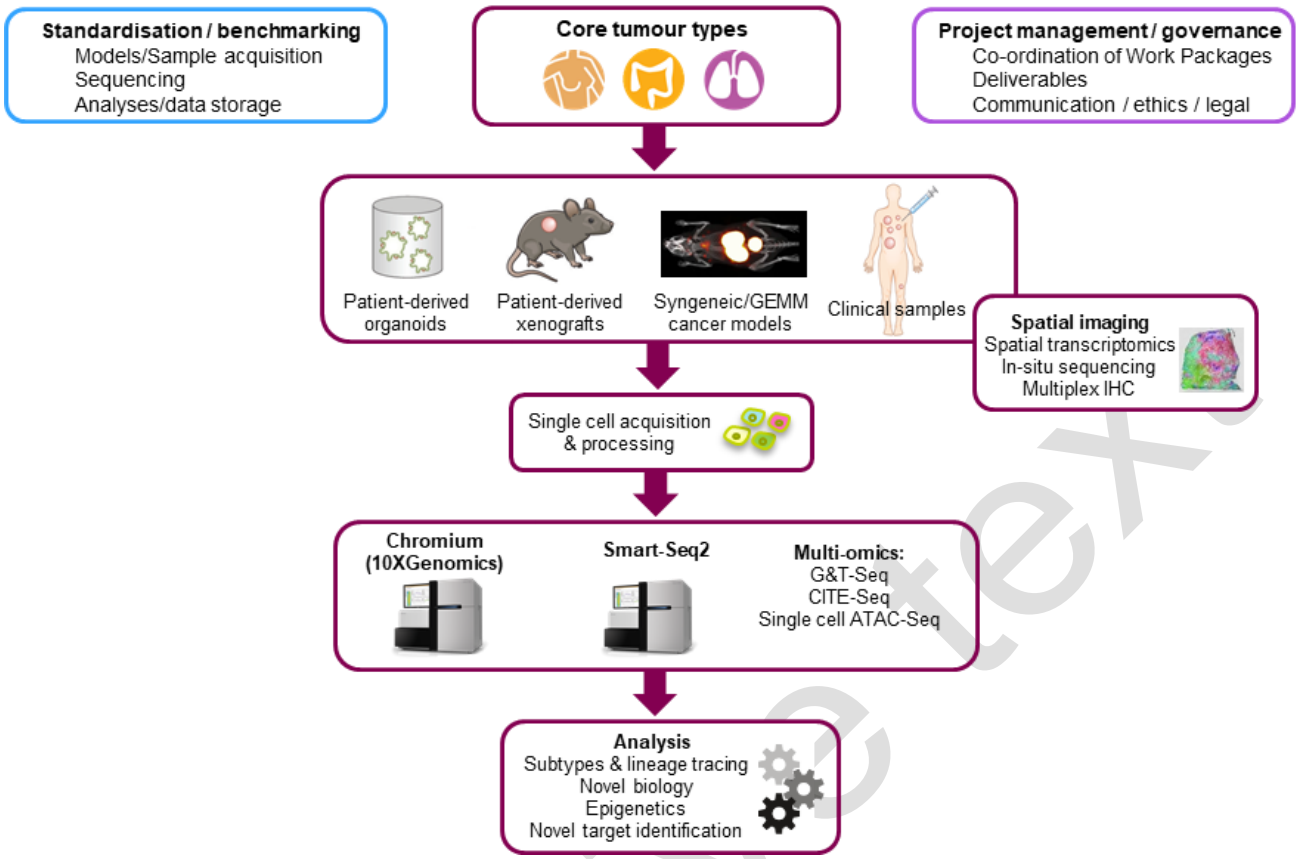

Figure 2. Work flow of the project. The various activities captured here form the basis for the 7 Work Packages detailed below.

Work Package 1 – Project management, coordination and long-term sustainability

Description: The goals of this work package are to support optimal project management in compliance with scientific and ethical standards, implement the strategy of the consortium, and ensure the appropriate dissemination of the project progress and outcomes.

Industry contribution: Project leader, coordination across different work packages (including overall scientific and strategic oversight).

Expected applicant consortium contribution: Project coordinator, project management expertise.

Work Package 2 – Portfolio management, coordination and prioritisation

Description: To direct and support optimal project delivery across tumour types, ensuring sufficient overlap that results are interpretable without wasteful duplication. To provide a mechanism for the identification and integration of bespoke test systems so that they have maximal impact.

- **Proposed objectives:**
- set up a review and selection process for models to resolve duplication between tumour type/drug treatments and ensure quality and technical standards (as defined in WP3) are met;
- provide additional models– PDO, PDX, GEMMs or patient samples – complementary to the EFPIA set.

Industry contribution: Portfolio leader, technical advice on the quality of studies that are proposed. Portfolio management expertise. Allocation and prioritisation of studies in a transparent way. Allocation of time and resources for appropriate technical development.

Expected applicant consortium contribution: Portfolio coordinator, technical advice on the quality of studies that are proposed. Allocation and phasing/timing of studies.

Work Package 3 – Standardisation and benchmarking of standard operating procedures

Description: To ensure the standardisation and benchmarking of protocols, raw and meta-data used across the consortium, both for sequencing technologies and analytics.

Industry contribution: Knowledge of PDO, PDX, GEMM and syngeneic models.

Expected applicant consortium contribution: Expertise in single-cell sequencing protocols and current gold standard analysis techniques, including data integration across platforms and studies.

Work Package 4 – Single cell acquisition from models of tumour plasticity

Description: The acquisition of high-quality single cells from the relevant tumour models that are suitable for single-cell sequencing.

Industry contribution: Expertise in the use of biological models for single cell provision (PDO, PDX, GEMM, Syngeneic). Drug treatment regimes *in vivo*. Industry will be the source of most of the single cells for study.

Expected applicant consortium contribution: Knowledge of best practice for processing single cells. Methods to avoid batch effects in collection and processing. Provision of single cells from additional pre-clinical and clinical models where appropriate.

Work package 5 – Single-cell sequencing

Description: The generation of high quality single-cell sequencing data from single cells acquired from each study

- **Proposed objectives should include:**
- high quality single-cell sequencing data in a format suitable for data Integration across studies (see work package below), using complementary technology platforms that are mature, well-supported and widely used;
- include specific single-cell sequencing technologies that address aspects of the epigenetic landscape of single cells (e.g. scATAC-seq) or cell surface protein expression (e.g. CITE-seq);
- evaluation and internalisation/uptake of new and emerging single cell techniques.

Industry contribution: Single-cell sequence data from internal platforms where available. Data upload and annotation from scRNAseq experiments.

Expected applicant consortium contribution: Expertise in single-cell sequencing, including alternate non-transcriptomic platforms (e.g. scATAC-seq, CITE-seq, G&T-seq) that are nominated to be included in specific studies. Expertise in evaluating new techniques and platforms. Data upload and annotation from scRNAseq experiments.

Work package 6 – Spatial imaging technologies

Description: To add spatial context to single-cell sequence data using a variety of spatial imaging technologies in order to validate the observed transcriptional changes from the single-cell sequencing studies, and to

understand the value of adding spatial orientation to these single cell observations. Apply to clinical samples as well as relevant pre-clinical models.

Industry contribution: Collection and curation of material from pre-clinical models as well as clinically relevant patient samples for analysis.

Expected applicant consortium contribution: Expert labs in spatial imaging of protein and transcript expression at single cell resolution.

Work package 7 – Analytical methods & integration of single cell datasets

Description:

a) To optimise/develop analytical methods and define the gold standard practice of single-cell sequencing data.
b) The integration of single-cell RNA-sequencing data and metadata/annotation across multiple platforms (including epigenetic), individuals, and studies and in addition to transfer information between datasets and spatial methods. Ultimately, to enable a more comprehensive comparison of cell populations in complex biological systems.
    - **Proposed objectives:**

- characterise the specific biological programs operative in Drug Tolerant Persister cells using single-cell sequencing datasets;
- integrate single-cell sequencing data across studies and technologies to capture common biological processes;
- identify novel drug targets.

Industry contribution: Pharma experience in novel target identification ligand affinity and druggability. IT expertise to support the data platform and analytics tools and ensure compatibility with industry requirements (e.g. FAIR requirements).

Expected applicant consortium contribution: Analysis expertise in single-cell sequencing data, both scRNA-seq as well as protocols addressing the epigenome. Expertise in data integration techniques, data storage solutions that allow interoperability. Academic experience in novel target ID.

Work package 8 – Communication/dissemination and ethics

Description:

a) to ensure effective communication and dissemination both within the consortium during the action, as well as external communication as appropriate with external synergy partners and stakeholders;
b) public engagement;
c) where clinical samples are to be used, appropriate planning and execution of correctly consented studies with corresponding ethical oversight and approval.

We anticipate that both industry and academic consortium partners will need to take full ownership and participation in this work package.

Additional considerations to be taken into account at the stage 2 full proposal

At stage 2, the consortium selected at stage 1 and the predefined industry consortium jointly submit the full proposal developed in partnership. The full proposal is based upon the selected short proposal at stage 1.

In the spirit of the partnership, and to reflect how IMI2 JU call topics are built on identified scientific priorities agreed together with EFPIA beneficiaries/large industrial beneficiaries, these beneficiaries intend to significantly contribute to the programme and project leadership as well as project financial management. The

final architecture of the full proposal will be defined by the participants in compliance with the IMI2 JU rules and with a view to the achievement of the project objectives. The allocation of a leading role within the consortium will be discussed in the course of the drafting of the full proposal to be submitted at stage 2. To facilitate the formation of the final consortium, until the roles are formally appointed through the consortium agreement, the proposed project leader from among EFPIA beneficiaries/large industrial beneficiaries shall facilitate an efficient negotiation of project content and required agreements. All beneficiaries are encouraged to discuss the project architecture and governance and the weighting of responsibilities and priorities therein.

Data management

In their stage 2 proposal, applicants should give due visibility to data management including use of data standards. A full 'data management plan' (DMP) as a distinct deliverable must be delivered within the first 6 months of the project. The DMP needs to be kept up to date with the needs of the project and as such be updated as necessary during its lifetime.[5]

Dissemination, exploitation and sustainability of results

In their stage 2 proposal, applicants must provide a draft plan for dissemination and exploitation, including sustainability of results. A full plan as a distinct deliverable must be delivered within the first 6 months of the project[6], and updated during the project lifetime. It could include identification of:

- different types of exploitable results;
- potential end-users of the results;
- results that may need sustainability and proposed sustainability roadmap solutions.

Sufficient resources should be foreseen for activities related to dissemination and exploitation, including the plan for the sustainability of the project results. This may involve engaging with suitable biological and medical sciences research infrastructures (RIs).[7]

Communication

The proposed communication measures for promoting the project and its findings during the period of the grant should also be described and could include a possible public event to showcase the results of the project.

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[5] Guidance on data management is available at http://ec.europa.eu/research/participants/docs/h2020-funding-guide/cross-cutting-issues/open-access-data-management/data-management_en.htm

[6] As an additional dissemination obligation under Article 29.1 of the IMI2 Grant Agreement will apply

[7] http://www.corbel-project.eu/about-corbel/research-infrastructures.html

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