485 RAFT: A FRAMEWORK TO SUPPORT RAPID AND REPRODUCIBLE IMMUNO-ONCOLOGY ANALYSES

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Background Analysis reproducibility and transparency are pillars of robust and trustworthy scientific results. The dependability of these results is crucial in clinical settings where they may guide high-impact decisions affecting patient health. Independent reproduction of computational results has been problematic and can be a burden on the individuals attempting to reproduce the results. Reproduction complications may arise from: 1) insufficiently described parameters, 2) vague methods, or 3) secret scripts required to generate final outputs, among others. Here we introduce RAFT (Reproducible Analyses Framework and Tools), a framework for immuno-oncology biomarker development built with Python 3 and Nextflow DSL2 which aims to enable end-to-end reproducibility of entire computational analyses in multiple contexts (e.g. local, compute cluster, or cloud) with minimal overhead through a focus on usability (figures 1 and 2).

Methods RAFT builds upon Nextflow's DSL2 module-based approach to workflows by providing a 'project' context upon which users can add metadata, load references, and build up their analysis step-by-step. RAFT also has pre-built modules with workflows commonly utilized in immuno-oncology analyses (e.g. TCR/BCR repertoire reconstruction and HLA typing) and aids users through automatic module dependency resolution. Transparency is gained by having a single end-to-end script containing all steps and parameters as well as a single configuration file. Finally, RAFT allows users to create and share a package of project metadata files including the main script, all input and output checksums, all modules, and the RAFT steps required to create the analysis. This package, coupled with any required inputs files, can be used to recreate the analysis or further expand an analysis with additional datasets or alternative parameters.

Results RAFT has been used by our computational team to create an immuno-oncology meta-analysis submitted to SITC 2020. A simple, proof-of-concept analysis has been used to establish RAFT's ability to support reproducibility by running locally on laptop computers, on multiple research compute clusters, and on the Google Cloud Platform.

Conclusions The RAFT platform shows promising capabilities to support rapid and reproducible research within the field of immuno-oncology. Several features remain in development and testing, such as incorporation of additional immunogenomics feature modules such as variant/fusion detection and HLA/peptide binding affinity estimation. Other functionality in development will enable collaborators to use remote Git repository hosting (e.g. GitHub or GitLab) to jointly and iteratively modify an analysis.

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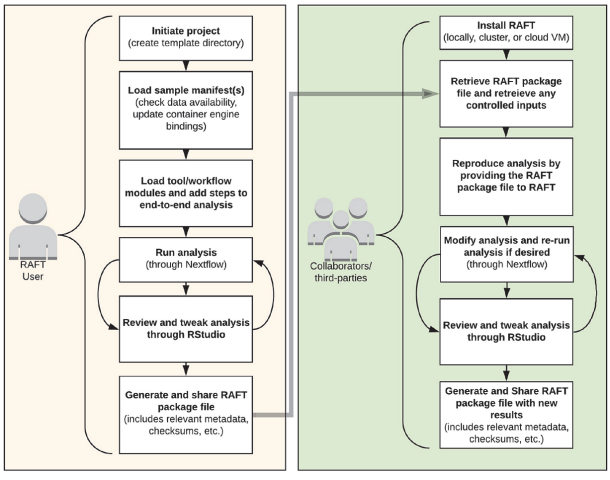
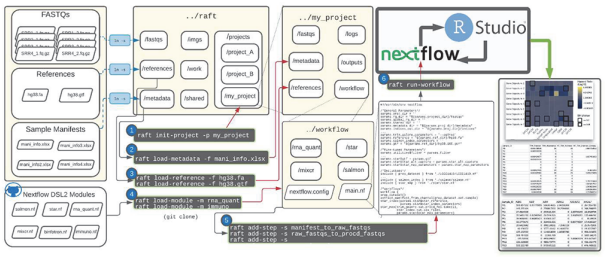


Abstract 485 Figure 1 Example RAFT Usage
Users define their required inputs, build their analysis, and run their analysis using the RAFT command-line interface. The metadata from the analysis can then be shared through a RAFT package with collaborators or interested third-parties in order to reproduce or expand upon the initial results.



Abstract 485 Figure 2 End-to-end RAFT
RAFT supports end-to-end analysis development through a 'project' structure. Users link local required files (e.g. FASTQs, references or manifests) into their appropriate/raft subdirectory. (1) Projects are initiated using the raft init-project command which creates and populates a project-specific directory. (2–3) Users then load required metadata (e.g. sample manifests or clinical data) and references (e.g. alignment references) into the project using the raft load-metadata or raft load-reference commands, respectively. (4) Modules consisting of tool-specific and topical workflows are cloned from a collection of remote repositories into the project using raft load-module. (5) Specific processes and workflows from previously loaded modules are added to the analysis (main.nf) through raft add-step. Users can then modify main.nf with their desired parameters and execute the workflow using raft run-workflow. (6) Additionally, RAFT allows an iterative approach where results from RAFT can be analyzed and modified through RStudio and re-run through Nextflow.

486 IRECEPTOR PLUS: A DATA INTEGRATION PLATFORM TO SHARE, COMPARE AND ANALYZE ADAPTIVE IMMUNE RECEPTOR REPERTOIRE (AIRR-SEQ) DATA FROM ANTIBODY/B- AND T-CELL REPERTOIRES

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Background Over the past few years, next-generation sequencing technologies have been developed to characterize 'adaptive immune receptor repertoires' (i.e., antibody/B-cell and T-cell receptor repertoires or AIRRs) in exquisite detail. AIRR sequencing (AIRR-seq) has enormous promise for understanding the dynamics of the immune repertoire in vaccinology, infectious diseases, autoimmunity, and cancer biology. While AIRR-seq data is important, it is also very large, complex, and requires specialized tools and services to curate, analyze, and share. In response to these challenges, The AIRR Community was formed in 2015 (www.airr-community.org). The AIRR Community comprises immunologists, immunogeneticists, computer scientists, bioinformaticians, and experts in legal, ethics and IP issues who are developing shared protocols and

standards to facilitate sharing and analysis of these repertoire data through the AIRR Data Commons (ADC).

Methods The iReceptor Gateway (www. ireceptor.org) implements the AIRR Data Commons as a network of federated repositories which facilitates data queries and advanced analyses. Secure data repositories, single cell immune profiling, and RNA gene expression and more detailed cell phenotype data for Systems Immunology are being added by the iReceptor Plus consortium, funded by Canadian Institutes of Health Research (CIHR) and the EU Horizon 2020 program.

Results As of August 2020, the iReceptor Gateway provides access to 2.7 billion receptor sequences, from 2779 repertoires, and 46 studies; these include 3 B-cell and 10 T-cell cancer studies. These can be queried for specific CDR3 sequences, in order to test whether particular sequences are public (occurring in multiple patients) or private (only found in a few individuals). These can also be queried for specific 'metadata', e.g. 'find all repertoires from studies of ovarian cancer.' The Gateway aggregates these repertoire data for further analysis by sophisticated AIRR-seq algorithms on HPC resources.

Conclusions Analysis of aggregated AIRR-seq data through the iReceptor Gateway has great potential to revolutionize many aspects of cancer immunotherapy. The FDA has already approved the use of AIRR-seq data for monitoring clonal expansion as a diagnostic tool in MRD (minimal residual disease). Sequences from tumor specific clones provide targets for monoclonal antibodies in anti-checkpoint therapy and CAR-T cell approaches. Several studies have shown that AIRR-seq data provide biomarkers that partition patients into responders/non-responders and predict those who may exhibit adverse reactions to novel cancer immunotherapies. This potential will be realized as more researchers adopt the AIRR Community standards for sharing and analyzing AIRR-seq data, resulting in more efficient biomedical research and improved patient care.

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Education and treatment management

487 REASONS FOR NOT TESTING FOR BIOMARKERS IN NON-SMALL CELL LUNG CANCER: A REGIONAL COMPARISON OF PATIENTS IN THE US AND EUROPE

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Background The growth in the number of targeted therapies available for the treatment of solid tumors has placed biomarker testing at the heart of clinical practice, especially for non-small lung cancer (NSCLC). Guidelines such as those by the American Society of Clinical Oncology and the European Society for Medical Oncology, recommend that all advanced NSCLC patients be tested for EGFR, ALK, ROS-1 and PD-L1 and that further markers (such as BRAF and KRAS) be included in larger panels. Despite these guidelines, oncologists do not always test NSCLC patients for these biomarkers. This study explores the reasons for not testing and compares these across the US, France, Germany, UK, Italy and Spain (collectively EU5) by examining real-world usage data.

Methods Between September and November 2019, a panel of oncologists (n=65 in US and n=235 in EU5) were asked to report on their practices relating to biomarker testing for 1,110 NSCLC patients through the submission of online, de-identified charts detailing testing for EGFR, ALK, ROS-1, PD-L1, BRAF, KRAS/NRAS, MET, RET, dMMR/MSI, TMB and NTRK. We collected data on 11,116 instances where biomarkers were skipped and recorded physicians' reasons for not testing (selected from a pre-coded list).

Results Of the reasons provided for not testing in the US (n=2,114) and EU5 (n= 9,002), waiting for progression was selected the most (27% and 25%, respectively). Lack of data regarding clinical utility (18% and 16%) and patients not meeting criteria (13% and 17%) were mentioned next as the top reasons for not testing across both regions. Compared to the US, EU5-based physicians had higher mentions of patients not meeting criteria (17% vs. 13%), tests not being reimbursed (7% vs. 5%) and treatment costs not being reimbursed (6% vs. 4%). The full distribution of reasons is shown in table 1 below.

Abstract 487 Table 1 Reasons for not testing

Table 1 *Reasons for not testing*	US (n=2,114)	EU5 (n=9,002)	UK (n=1,876)	FR (n=1,672)	DE (n=1,446)	IT (n=2,035)	ES (n=1,973)
Denotes significant difference at p<0.05	U	A	B	C	D	E	F
Will only test after progression	27%	25%	32%^{CDEF}	24%	25%^{F}	27%^{F}	20%
Lack of data regarding clinical utility	18%^{A}	16%	17%	18%^{F}	18%^{F}	16%	14%
Patient did not meet criteria	13%^{A}	17%	19%^{EF}	17%^{E}	26%^{BCEF}	12%	15%
Lack of targeted therapies for this test	6%	7%	6%	6%	13%	6%	7%
Test not reimbursed	5%^{A}	7%	9%^{CDE}	4%	6%	6%	10%^{CDE}
Cost of testing	5%	5%	5%^{DF}	8%^{ABDF}	2%	6%^{DF}	2%
Treatment cost / drug not reimbursed	4%^{A}	6%	10%^{CDEF}	3%	5%	6%^{C}	7%^{C}
Patient tested positive for other markers	4%^{A}	7%	3%	7%^{B}	13%^{BCE}	6%^{B}	10%^{BCE}

Conclusions Despite recommendations in guidelines, physicians in the US and EU5 often forgo testing to wait until after progression, because of a perceived lack of clinical utility or because they deem the patient ineligible for testing. While individual countries differ on their approaches to testing - some are more cost sensitive (UK, France) while others are more discerning as to which patients are eligible for testing (Germany) - a concerted effort is needed to educate physicians on the clinical utility of biomarker testing.

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488 THE IMPACT OF EDUCATION ON NOVEL CONCEPTS IN METASTATIC MELANOMA: TRIPLET THERAPY

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Background Advanced melanoma treatment selection is guided by BRAF-mutation status and patient and disease-specific factors. Historically, oncologists decided between targeted therapy or immune checkpoint inhibitors (ICI). However, given the differences in onset of activity, response durability, and adverse