The AIRR Data Commons: 4 billion reasons to store, analyze and share antibody/B-cell and T-cell receptor repertoire data



Today's speakers

- Dr. Felix Breden
 - Executive Director, iReceptor/iReceptor Plus, Simon Fraser University
 - Member and former chair, AIRR Community Executive
- Dr. Brian Corrie
 - Technical Director, iReceptor/iReceptor Plus, Simon Fraser University
 - Co-chair, AIRR Common Repository Working Group
- Dr. Kira Neller
 - Data curator/bioinformatician, iReceptor/iReceptor Plus, Simon Fraser University
 - Member, AIRR Standards Working Group
- Dr. Scott Christley
 - Computational Biologist, UT Southwestern Medical School
 - Project Leader, VDJServer
 - Co-chair, AIRR Standards Working Group

Today's Webinar

Part I: Adaptive Immune System and the AIRR Community

Part II: The AIRR Data Commons

Part III: AIRR Data Commons Tool Demos

•*iReceptor Gateway*

•AIRR-seq Data Curation

•VDJServer Analysis Portal

Part I: Adaptive Immune System and the AIRR Community

Adaptive Immune System

- Comprises antibodies/B-cell receptors and T-cell receptors AIRR-seq data (Adaptive Immune Receptor Repertoire)
- Incredibly variable to recognize and *remove* bacteria and viruses (including new ones, *e.g.* novel coronavirus)
- Also, must recognize and *not remove* >25,000 expressed "self" proteins
- Basis of vaccines, drugs suppressing autoimmune diseases, new cancer immunotherapies, *etc*.

Why a platform specific to AIRR-seq data? AIRR-seq data are difficult to share and compare:

Size of data sets

AIRR-seq repertoires are highly diverse: ~10¹³ potential human B-cell receptors

Individual can have ~10⁹ B cells and T cells: 10⁶ or 10⁷ receptors sequenced per sample

Studies produce huge data sets:

Burkitt lymphoma (Lombardo *et al*.) – 1.2B B-cell receptors Systemic sclerosis (de Bourcy *et al*.) - 700M B-Cell receptors Several recent cancer studies – >500M T-cell receptors AIRR-seq data are difficult to share and compare: VDJ recombination demands unique data base model for annotated receptor sequences



Clones are sets of B-cells or T-cells descended from ancestral cell produced by V(D)J recombination

Immunoglobulin and T-cell Receptor genes are only genes in eukaryote genome that undergo this somatic recombination

AIRR-seq data are difficult to share and compare: Many ways for experiments to differ!



Yaari & Kleinstein 2015 Genome Medicine 7:121-135

AIRR-seq data are difficult to share and compare: Complexity and confidentiality of data sets

Require data on patient demography, treatment, clinical outcome, etc.

Complex analyses demand unique bioinformatic tools

AIRR-seq data could lead to personal identification?

B-cell Clonal Lineage Expansion in Health and Disease

CLL sample 5 26,086 sequences total 48.0 % maximum cluster

Healthy donor 1 12,316 sequences total 0..49 % maximum cluster



Chronic Lymphocytic Leukemia (CLL) is characterized by expansion of a few dominant clones in B-cell repertoire (Bashford-Rogers *et al.* 2019)

FDA approved Adaptive Biotechnologies clonoSEQ[®] test for Minimal Residual Disease (MRD) based on searching for these CLL-associated, expanded clones

Patterns Observed in COVID-19 patient AIRR-seq data repository: 20 studies, 3531 repertoires, 1B sequences

- Stereotypical immune response mediated by convergent clonotypes
 - Galson et al., Montague et al., Nielsen et al., Robbiani et al., Sokal et al., Xiang et al. Zhang et al.
 - Adaptive Biotechnologies FDA approved T-Detect COVID test for prior infections
- Pre-existing immunity in unexposed individuals
 - Precursor nABs: Kreer et al., Mor et al.
 - SARS-CoV-2 T-cell epitopes cross-reactive to common viruses: Mahajan et al., Grifoni et al., Zhao et al.
- Neuro-COVID
 - 7 studies from ADC show T-cell expansion in "long haulers" with neurological defects: Hemming et al.
- Biased V-gene usage
 - IGHV3-53 and IGHV3-66 greatly increased in anti-SARS-CoV-2 antibodies: Kim et al., Mor et al., Barnes et al.
 - T-cell repertoires biased toward specific TRVB genes in severe hyper-inflammatory COVID-19 patients: Cheng et al.

Adaptive Immune Receptor Repertoire (AIRR) Community

The AIRR Community is a global, grass-roots group of immunologists, bioinformaticists, computer scientists, experts in legal, ethical and IP issues, who are developing guidelines and standards for the generation, annotation and storage of high-throughput AIRR-seq data to facilitate its use by the larger research community.

Ability to share AIRR-seq data greatly increases the value of any one data set: -each researcher, small N, large amount of data per sample

- -increase sample sizes, statistical power
- -AI approaches demand huge sample sizes
- -facilitate comparisons between affected/controls/multiple disease states

AIRR Community Working Groups

- 1. Minimal Standards for publishing or depositing AIRR-seq data (MiAIRR)
- 2. Data Representation common formats for annotated data
- 3. Software interoperability of analysis software
- 4. Common Repository Data Commons for AIRR-seq data, following FAIR principles
- 5. Diagnostics develop diagnostics and markers for disease; one goal is sustainable business model
- 6. Legal and Ethics standards for human subjects
- 7. Biological Resources testing molecular protocols
- 8. Germline Database inference from AIRR-seq data

AIRR Community Working Groups Develop Standards



Standards (Publications) must be ratified by full AIRR Community

Join: www.airr-community.org

Part II: The AIRR Data Commons

Making AIRR-seq data FAIR and TRUSTed

- Goal of the AIRR Community:
 - Promote the Reproducibility and Reuse of AIRR-seq data (Breden et al., 2017)

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 - Find data of interest from multiple labs/institutions
 - Combine the data of interest (Accessible and Interoperable)
 - Reuse combined data in new analyses to derive new insights (FAI leads to Reuse)

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- Reproducible science requires **TRUST**ed AIRR-seq data repositories
 - Transparent, Responsible, User focused, Sustainable, and Technologically reliable
 - Community involvement is critical to gaining TRUST The AIRR Community

• Network of distributed AIRR-seq repositories

AIRR Data Commons International network of distributed repositories



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 - 4 repositories, 60 studies, 4 billion sequences

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 - MiAIRR Standard for study reporting
 - Rubelt et al. (Nat. Immunol., 2017)
 - File formats for data sharing
 - Vander Heiden et al. (Front. Immunol., 2018)
 - Queryable through ADC web API
 - Christley et al. (Front. Big Data, 2020)

AIRR Data Commons International network of distributed repositories



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iReceptor Scientific Gateway Interactive web-based data discovery, exploration, and analytics



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iReceptor Scientific Gateway Interactive web-based data discovery, exploration, and analytics



Web based portal that hides the complexity of finding, searching and federating data across many repositories! AIRR Data Commons

International network of distributed repositories



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Data Query



Web based portal that hides the complexity of finding, searching and federating data across many repositories!

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Data Query

Data

- The ADC continues to grow...
 - We encourage everyone to share!
- 4 billion reasons to use the ADC!
 - 60 studies, 4 billion sequences



AIRR Data Commons Growth

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 - 60 studies, 4 billion sequences
 - 15 COVID-19 studies, 1 billion sequences
 - Neilsen et al. data available June 2020
 - Preprint, May 2020, Cell Host & Microbe, Oct 2020



AIRR Data Commons Growth

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- 4 billion reasons to use the ADC!
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 - Neilsen et al. data available June 2020
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- Data reuse is becoming common
 - Partially driven by COVID-19 data
 - Schultheiß et al. (Immunity, Aug 2020) Data
 - Meysman et al. (bioRxiv, Sep, 2020) Reuse
 - Heming et al. (Immunity, Jan 2021) Reuse
 - Chang et al. (Front. Immunol., Apr 2021) Reuse
 - Data reuse = paper citations!



AIRR Data Commons Growth

- Because everyone is doing it...
 - Significant user increase in last 12 months
 - Critical mass of data? COVID-19?





How do I use the AIRR Data Commons?

- iReceptor Gateway Search and ye shall find!
 - Search 60 studies for over 80 MiAIRR study/subject/sample metadata fields
 - E.g. Finding COVID-19 data...



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• Simple analyses are trivial - Gene usage, CDR3 length distributions



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 - Use the ADC API directly through the command line or code Full search and download power

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 - Find a SARS-CoV2 specific antibody and get its CDR3 (e.g. 0304-2F8 ARDLYYYGMDV)

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 - Use the ADC API and "curl" to find out which v-call is associated with this CDR3 in the ADC

```
Query
curl -d '
{
    "filters": {
        "op":"contains","content":
        {
        "field":"junction_aa", "value":"ARDLYYYGMDV"
      }
    },
    "fields":["v_call","junction_aa"]
}' http://covid19-1.ireceptor.org/airr/v1/rearrangement
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 - Use the ADC API and "curl" to find out which v-call is associated with this CDR3 in the ADC
 - Found in data from 5 COVID-19 studies across 21 subjects

Query

```
curl -d '
{
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      }
    },
    "fields":["v_call","junction_aa"]
}' http://covid19-1.ireceptor.org/airr/v1/rearrangement
```

Response (partial)

```
...
```

```
{ "junction_aa": "CARDLYYYGMDVW", "v_call": "IGHV3-53*04"},
{ "junction_aa": "CARDLYYYGMDVW", "v_call": "IGHV3-53*01"},
{ "junction_aa": "CARDLYYYGMDVW", "v_call": "IGHV3-66*02"},
{ "junction_aa": "CARDLYYYGMDVW", "v_call": "IGHV3-53*01"},
```

- Analyze the data you find in the ADC
- The AIRR Software compliance badge
 - Requirements
 - Open source, support AIRR Standards, example data, containerization, user support
 - <u>https://docs.airr-community.org/en/stable/swtools/airr_swtools_standard.html</u>
- Current AIRR certified analysis tools:
 - Sonar (Schramm et al. Front Immunol, 2016)
 - ImmuneDB (Rosenfeld et al. Front Immunol, 2018)
 - Scirpy (Sturm et al. Bioinformatics, 2020)
 - Immcantation (Vander Heiden et al. Bioinformatics, 2014)
 - Your tool goes here...



How do I share data in the AIRR Data Commons?

- Reach out to your colleagues in the AIRR Community
 - We can help!
- Run your own repository (iReceptor Turnkey)
 - Docker containers, simple to install and run (Github download)
 - <a>www.ireceptor.org/repositories#turnkey
- Upload your data to an existing repository (VDJServer)
 - Upload data, run it through the VDJServer pipeline, publish!
 - <u>www.vdjserver.org</u>





What is next for the AIRR Data Commons?

- AIRR extensions to the standard coming soon to a repository near you!
 - Clones and clonal lineages
 - Single cell capabilities
- More advanced analyses iReceptor Plus (<u>www.ireceptorplus.org</u>)
 - Extensions to existing Statistics capabilities
 - Don't just download Integrated AIRR analysis tools
 - E.g. Run Immcantation analysis on data in the ADC
 - Never leave the web based UIs (iReceptor Gateway, VDJServer)



Part III: AIRR Data Commons Tool Demos

The iReceptor Gateway



Username

Password

kira neller

A science gateway that enables the discovery, analysis and download of AIRR-seq data (antibody/B-cell and T-cell receptor repertoires) from multiple independent repositories (the AIRR Data Commons), including:

- iReceptor Public Archive P
- VDJServer

5 STUDY TYPES

Study

Case=

Study

24 TISSUES

venous breast

blood

blood









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Othe

None

DNA

RNA

Using the iReceptor Gateway: home page



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4 remote repositories, 49 research labs, 60 studies

 \times





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- <u>AIRR COVID-19</u>
- VDJServer ₽

5 STUDY TYPES

Observational Study Othe

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MiReceptor Search-

Help - admin - kira_neller -



About iReceptor

Our Mission

iReceptor facilitates the curation, analysis and sharing of antibody/B-cell and T-cell receptor repertoires (Adaptive Immune Receptor Repertoire or AIRR-seq data) from multiple labs and institutions. We are committed to providing a platform for researchers to increase the value of their data through sharing with the community. This will greatly increase the amount of data available to answer complex questions about the adaptive immune response, accelerating the development of vaccines, therapeutic antibodies against autoimmune diseases, and cancer immunotherapies.

Getting Started

- Displaying repertoire statistics @
- Finding COVID-19 data &
- Finding B-cell or T-cell repertoires Image: Finding B-cell or T-cell repertoires
- Finding sequences using a specific V-Gene Image of the sequ
- <u>Downloading sequences</u> If
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See the iReceptor Gateway documentation & for more.

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Individual Repertoires 1-120 of 6110 Customize displayed columns

🛃 TSV **J**SON

Browse sequences from 6110 repertoires \rightarrow

kira neller-

Stats	Repository	Study title 🛛 🛛 👫	Diagnosis 😧 🎵	Study group 🥹 🔱	Sequences 1	Lab name 😧 🛛 👫	Tissue 🥹 ↓↑	PCR target 🛛 🗍	Cell subset 🛛 🛛 👫	Cell subset phenotype 😧 ↓
ılı 🔰	AIRR COVID-19	<u>Minervina et al., Lo</u>	COVID-19	Case	229,933	Mora Lab, Laboratoir	blood	TRA	CD8-positive, alpha	CD8+
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Customize displayed columns X Close

Repertoire

- Repertoire Description
- O
 Repertoire ID
- Repertoire Name

Study

- Contact (collection)
- Contact (deposition)
- G Funding
- Inclusion criteria
- Cab address
- 🗹 😧 Lab name
- Publications
- Study Description
- 🗹 😧 Study ID
- Study keywords
- Study title
- Study type
- Study type (Ontology ID)

Subject

- Age (deperecated)
- Age event
- Age maximum
- 🗌 😧 Age minimum
- 🗌 🚱 Age unit

Age unit (Ontology ID)

- Ancestry
 Ethnicity
 - Organism
- Organism (deprecated)
- Organism (deprecated)
- Organism (Ontology ID)
- 🗆 😧 Race
- □ ② Relation (subjects)
- Relation type
- 🗆 😧 Sex
- Strain name
- 🗹 😧 Subject ID
- Synthetic library

Sample

- 🗆 🛿 🖓 Anatomic site
 - 🗆 🛿 Biomaterial provider
- Collection event
- Ollection time
 Disease state
- Sample ID
- Sample type
- Sample ty
- 🔽 😧 Tissue
-] 3 Tissue (Ontology ID)

- Diagnosis
- Oiagnosis
- Diagnosis (Ontology ID)
- 🗌 🛿 Disease stage
- Immunogen/agent
- O Intervention
- Constant of disease
- O
 Medical history
- Prior therapies
- 🔽 😧 Study group

Cell Processing

- Ø # cells/experiment
- Ø # cells/sequencing reaction
- Cell isolation procedure
- Cell quality
- Cell species
- Cell species (Ontology ID)
- 🗆 😧 Cell storage
- 🗹 😧 Cell subset
- Cell subset (Ontology ID)
- Cell subset phenotype
- Processing protocol
- □ 3 Single-cell sort
- Tissue processing

- Nucleic Acid Processing
- Complete sequences
- O Library generation method
- C library generation protocol
- Linkage of loci
- Protocol IDs
- Target substrate
- In the second secon
- Template amount

Sequencing Run

- Batch number
- Date of sequencing run
- Reads passing QC
- Sequencing facility
- Sequencing kit
- Sequencing platform

Data Processing

- 🗌 😧 Analysis ID
- Collapsing method
- Data processing ID
- O Data processing protocols
- Paired read assembly
- Primary annotation
- Primer match cutoffs

- Processed files
- Quality thresholds

Sample Processing

Raw Sequence Data

German Provide the second second

Paired read direction

Sequencing file name

Sequencing file type

O Forward PCR target

Reverse PCR target

□ ② Paired sequencing file name

Paired read length

Read direction

PCR Target

Other

PCR target

Repository

Sequences

Software tools/versions
 V(D)J germline database

Sample Processing ID

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±JSON ±TSV

Browse sequences from 6110 repertoires \rightarrow

Stats	Repository	Study title 🛛 🛛 🕸	Diagnosis 🤪 \downarrow 🕇	Study group 🕘 🔱	Sequences 1	Lab name 😧 🛛 👫	Tissue 🛛 🗍	PCR target 😧 🗍	Cell subset 🛛 🛛 🔓	Cell subset phenotype 😧 🕽
ılı 👘	AIRR COVID-19	<u>Minervina et al., Lo</u>	COVID-19	Case	229,933	Mora Lab, Laboratoir	blood	TRA	CD8-positive, alpha	CD8+
ılı 👘	AIRR COVID-19	Nolan et al., COVID			98,230	Adaptive Biotechnolo	blood	TRB		
ılı	AIRR COVID-19	Nolan et al., COVID	COVID-19	Case	83,967	Adaptive Biotechnolo	blood	TRB		
ılı	AIRR COVID-19	Nolan et al., COVID	COVID-19	Case	194,683	Adaptive Biotechnolo	blood	TRB		
ılı 👘	AIRR COVID-19	Nolan et al., COVID	COVID-19	Case	71,321	Adaptive Biotechnolo	blood	TRB		
ılı 👘	AIRR COVID-19	Nolan et al., COVID	COVID-19	Case	27,389	Adaptive Biotechnolo	blood	TRB		
ılı 🔰	AIRR COVID-19	Nolan et al., COVID	COVID-19	Case	91,860	Adaptive Biotechnolo	blood	TRB		
ılı 👘	AIRR COVID-19	Nolan et al., COVID	COVID-19	Case	134,902	Adaptive Biotechnolo	blood	TRB		
ılı 👘	AIRR COVID-19	Nolan et al., COVID	COVID-19	Case	157,489	Adaptive Biotechnolo	blood	TRB		
ılı	AIRR COVID-19	Nolan et al., COVID	COVID-19	Case	150,840	Adaptive Biotechnolo	blood	TRB		
ılı 👘	AIRR COVID-19	Nolan et al., COVID	COVID-19	Case	236,319	Adaptive Biotechnolo	blood	TRB		
ılı	AIRR COVID-19	Nolan et al., COVID	COVID-19	Case	105,620	Adaptive Biotechnolo	blood	TRB		
ılı	AIRR COVID-19	Nolan et al., COVID	COVID-19	Case	63,558	Adaptive Biotechnolo	blood	TRB		



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Browse sequences from 6110 repertoires \rightarrow

Stats	Repository	Study title 😧 🛛 👫	Diagnosis 😧 🎵	Study group 🥹 🔱	Sequences 1	Lab name 🥹 🛛 👫	Tissue Ø ↓↑	PCR target 😧 🗍	Cell subset 😧 🛛 👫	Cell subset phenotype 😧 ↓
ılı 🔰	AIRR COVID-19	<u>Minervina et al., Lo</u>	COVID-19	Case	229,933	Mora Lab, Laboratoir	blood	TRA	CD8-positive, alpha	CD8+
ılı	AIRR COVID-19	Nolan et al., COVID			98,230	Adaptive Biotechnolo	blood	TRB		
-di	AIRR COVID-19	Nolan et al., COVID	COVID-19	Case	83,967	Adaptive Biotechnolo	blood	TRB		
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li	AIRR COVID-19	Nolan et al., COVID	COVID-19	Case	71,321	Adaptive Biotechnolo	blood	TRB		
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li	AIRR COVID-19	Nolan et al., COVID	COVID-19	Case	157,489	Adaptive Biotechnolo	blood	TRB		
d i	AIRR COVID-19	Nolan et al., COVID	COVID-19	Case	150,840	Adaptive Biotechnolo	blood	TRB		
ılı	AIRR COVID-19	Nolan et al., COVID	COVID-19	Case	236,319	Adaptive Biotechnolo	blood	TRB		
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ılı 🕺	AIRR COVID-19	Nolan et al., COVID	COVID-19	Case	63,558	Adaptive Biotechnolo	blood	TRB		

Filters

Full-text search @

covid-19	
Filter by study	+
Filter by subject	+
Filter by sample	+
More filters	+

-liters		Filter by study
Full-text search 😧		Study ID 😧
COVID-19		
Filter by study	+	Study title 😧
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More filters	+	Study group 2

Filter by study	-
Study ID 😧	
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Any	-
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[Apply filters \rightarrow

Filters

Full-text search 😧	
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Filter by study	+
Filter by subject	+
Filter by sample	+
More filters	- +

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Filter by study	-
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Study group 😧	
Lab name 😧	
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Filter by subject	-
Subject ID 😧	
Organism 😧	
Any	•
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Any	•
Ethnicity 😧	
Any	-
Age minimum 9	Age maximum 😧
Diagnosis 😧	
Any	•
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Filters

Full-text search 😧	
covid-19	

Filter by study	- 1
Filter by subject	- 4
Filter by sample	- 4
More filters	- 4

Filter by study	-
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	Apply litters \rightarrow

Filter by subject	-
Subject ID 😧	
Organism 😧	
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	Apply filters \rightarrow

Filter by sample			
Sample ID 😧			
PCR target 😧			
Any -			
Cell subset 😧			
Any 🗸			
Tissue 😧			
Any -			
Target substrate 😧			
Any 🗸			
Cell subset phenotype 😧			
Sequencing platform 😧			

Apply filters \rightarrow

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Study Contact (deposition)	
Study Funding	
Study Inclusion criteria	
Study Lab address	
Study Publications	
Study Study Description	
Study Study keywords	

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Repertoire Repertoire Description				
Repertoire Repertoire ID				
Repertoire Repertoire Name				
Study Contact (collection)				
Study Contact (deposition)				
Study Funding				
Study Inclusion criteria				
Study Lab address				
Study Publications				
Study Study Description				
Study Study keywords				

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More filters –
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Study Contact (collection)
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Study Funding
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Study Lab address
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More filters -	More
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More filters		
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	Apply filters	
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Add a filter Repertoire F	Repertoire ID	→ ~

Using the iReceptor Gateway: Filtered Results



Using the iReceptor Gateway: Filtered Results



Using the iReceptor Gateway: Filtered Results



Using the iReceptor Gateway: Statistics

Repertoire: Pt-6 - Pt-6-2 - TRB



×

Study	Subject	Sample	Sequences
Study title: Schultheiß et al., Next	Subject ID: Pt-6	Sample ID: Pt-6-2	Rearrangement Count: 83,468
<u>Generation Sequencing of T and</u> B cell receptor repertoires from	Diagnosis: COVID-19	Cell subset:	
COVID-19 patients showed	Age: 60-69 years	PCR target: TRB	
<u>signatures associated with</u> <u>severity of disease</u>	Sex: female	Tissue: blood	

Study group: Case
Using the iReceptor Gateway: Browsing Sequences



Using the iReceptor Gateway: Browsing Sequences



Using the iReceptor Gateway: Browsing Sequences



Using the iReceptor Gateway: Downloading Sequences

iReceptor	Search -	1. Repertoire Metadata	2. Sequences				Help → admin →	kira_neller -	
2. Sequence Sea Filter by sequence and seque	Irch ence annotati	on feature							
Filters		Active filters							
Filter by VDJ	+	Repertoire Metadata filters: Full-text	Go back to Repertoire Metadata Sea	rch				rk this search	
Filter by Junction AA	+	Search results statistics	Search results statistics						
Advanced filters	+	83,468 sequences (1 repertoire) returned from 1 remote repository, 1 research lab and 1 study.							
		1 STUDY TITLE	1 SUBJECT ID	1 SAMPLE ID	1 DIAGNOSIS	1 TISSUE	1 PCR TAF	RGET	
		Schultheiß et a	Pt-6	Pt-6-2	COVID-19	blood	TRB		
		Individual Sequences 1-10) of 83 thousand Customize displayed	columns			L Download all 83,46	8 sequences	
		V Gene With Allele 😧	D Gene With Allele 🚱	J Gene With Allele 🚱	Junction/CDR3 AA 😧	Juno	tion Length (AA) 😧		

V Gene With Allele 😡	D Gene With Allele 😧	J Gene With Allele	Junction/CDR3 AA 😧	Junction Length (AA) 😧
TRBV5-1*00	TRBD2*00	TRBJ2-1*00	CARCWTSGGVNDDQFF	16
TRBV30*00	TRBD2*00	TRBJ2-2*00	CAWAGGQGGELFF	13
TRBV11-1*00	TRBD1*00	TRBJ1-1*00	CASSLEGTGFEAFF	14
TRBV18*00		TRBJ2-3*00	CASSVGG_TDTQYF	14
TRBV29-1*00	TRBD1*00	TRBJ1-1*00	CSALPGQLEAFF	12
TRBV27*00	TRBD2*00	TRBJ2-3*00	CASSLGTSGGDTQYF	15
TRBV6-5*00	TRBD1*00	TRBJ1-2*00	CASSPVTGTGHYGYTF	16
TRBV19*00		TRBJ1-1*00	CASSNMGSGTEAFF	14
TRBV29-1*00		TRBJ2-1*00	CSVEPTRGWVGPYNEQFF	18
TRBV6-1*00		TRBJ1-6*00	CASSEETDWPNSPLHF	16

Using the iReceptor Gateway: Downloading Sequences

iReceptor	Search -	1. Repertoire Metadata	2. Sequences				Help			
2. Sequence Sea Filter by sequence and seque	arch ence annotati	on feature								
Filters		Active filters								
Filter by VDJ	+	Repertoire Metadata filters: Full-tex	xt search Go back to Repertoire Metadata Sear	ch						
Filter by Junction AA	+	Search results statistics	Search results statistics							
Advanced filters	+	83,468 sequences (1 repertoire	e) returned from <u>1 remote repository</u> , <u>1 res</u>	earch lab and 1 study.						
		1 STUDY TITLE	1 SUBJECT ID	1 SAMPLE ID	1 DIAGNOSIS	1 TISSUE	1 PCR TARGET			
		Schultheiß et a	Pt-6	Pt-6-2	COVID-19	blood	TRB			
		Individual Sequences 1-	10 of 83 thousand 🖸 Customize displayed (columns			L Download all 83,468 sequences			
		V Gene With Allele 😧	D Gene With Allele	J Gene With Allele 😧	Junction/CDR3 AA 😧	Juncti	on Length (AA) 😧			
		TRBV5-1*00	TRBD2*00	TRBJ2-1*00	CARCWTSGGVNDDQFF	16				
		TRBV30*00	TRBD2*00	TRBJ2-2*00	CAWAGGQGGELFF	13				
		TRBV11-1*00	TRBD1*00	TRBJ1-1*00	CASSLEGTGFEAFF	14				
		TRBV18*00		TRBJ2-3*00	CASSVGG_TDTQYF	14				
		TRBV29-1*00	TRBD1*00	TRBJ1-1*00	CSALPGQLEAFF	12				
		TRBV27*00	TRBD2*00	TRBJ2-3*00	CASSLGTSGGDTQYF	15				
		TRBV6-5*00	TRBD1*00	TRBJ1-2*00	CASSPVTGTGHYGYTF	16				
		TRBV19*00		TRBJ1-1*00	CASSNMGSGTEAFF	14				
		TRBV29-1*00		TRBJ2-1*00	CSVEPTRGWVGPYNEQFF	18				
		TRBV6-1*00		TRBJ1-6*00	CASSEETDWPNSPLHF	16				

Search -

Help - admin - kira_neller -



About iReceptor

Our Mission

iReceptor facilitates the curation, analysis and sharing of antibody/B-cell and T-cell receptor repertoires (Adaptive Immune Receptor Repertoire or AIRR-seq data) from multiple labs and institutions. We are committed to providing a platform for researchers to increase the value of their data through sharing with the community. This will greatly increase the amount of data available to answer complex questions about the adaptive immune response, accelerating the development of vaccines, therapeutic antibodies against autoimmune diseases, and cancer immunotherapies.

Getting Started

- <u>Displaying repertoire statistics</u> IP
- Finding COVID-19 data &
- Finding B-cell or T-cell repertoires Image: Finding B-cell or T-cell repertoires
- Finding sequences using a specific V-Gene &
- <u>Downloading sequences</u> If
- Frequently Asked Questions &

See the iReceptor Gateway documentation & for more.

Search -

Help - admin - kira_neller -



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- Frequently Asked Questions &

See the iReceptor Gateway documentation & for more.

Sequence Quick Search

Find sequences through all repositories with a specific Junction/CDR3 AA substring.

Junction/C	DR3 AA 😧	Cell subset 😧
ARDLYYY	/GMDV	Any -
Organism (9	
Any	\sim	Search

IGHV3-53*04

iReceptor	Search -	Sequence Quick Search					Help -	admin▼	kira_neller-
Sequence Quick Filter by sequence and sequ	Search	on features (e.g. Junction)							
Filters		Active filters							
Junction/CDR3 AA 9		★ Junction/CDR3 AA Remove all filters						🖈 Bookm	ark this search
ARDLYYYGMDV	ARDLYYYGMDV Search results statistics								
		906 sequences (89 repertoires) return	ned from <u>4 remote repositories</u> , <u>11 re</u>	search labs and 12 studies.					
Sample level filters	-	12 STUDY TITLES	39 SUBJECT IDS	89 SAMPLE IDS	4 DIAGNOSE	S 5 TISSUES		2 PCR TA	ARGETS
Organism 😧		Apublic			COVID-10				
Any	~	database Of Other	Other	Other	Comb-12		and		
Cell subset 😧 Any	•	et al., Deep Uniqueness, commonal	AT0008_0019_01 326797 326780	Covid_Barts_19 Covid_Barts_15 Covid_Barts_05	rse Ipr None	ondary Ogressive venous blood	ther	IGH	IGL
Apply f	filters →	Individual Sequences 1-31 of 9	06 Customize displayed columns				L [ownload all 9	006 sequences
		V Gene With Allele 😧	D Gene With Allele	J Gene	e With Allele 😧	Junction/CDR3 AA 😧	Junctio	n Length (AA	A) 🥹
		IGHV1-8*01		IGHJ6*	02	CARDLYYYGMDVW	13		
		IGHV3-53*02, or IGHV3-53*01		IGHJ6*	02	CARDLYYYGMDVW	13		
		IGHV3-53*02, or IGHV3-53*01		IGHJ6*	02	CARDLYYYGMDVW	13		
		IGHV3-74*01		IGHJ6*	02	CARDLYYYGMDVW	13		
		IGHV3-53*02, or IGHV3-53*01		IGHJ6*	02	CARDLYYYGMDVW	13		
		IGHV3-53*02, or IGHV3-53*01		IGHJ6*	02	CARDLYYYGMDVW	13		
		IGHV3-53*02, or IGHV3-53*01		IGHJ6*	02	CARDLYYYGMDVW	13		
		IGHV3-21*04		IGHJ6*	02	CARDLYYYGMDVW	13		
		IGHV3-64*01		IGHJ6*	02	CARDLYYYGMDVW	13		

IGHJ6*02

13

CARDLYYYGMDVW

Part III: AIRR Data Commons Tool Demos

AIRR-seq Data Curation

Curating an AIRR-seq study for the ADC

What you need...

Rearrangement annotation files

- One per repertoire, in AIRR.tsv format
- <u>https://docs.airr-community.org/en/stable/datarep/format.html</u>

Metadata

- One file for the study, following MiAIRR Reporting Standards
- <u>https://docs.airr-community.org/en/stable/miairr/data_elements.html</u>



Curating an AIRR-seq study: MiAIRR



Curating an AIRR-seq study: MiAIRR



Curating an AIRR-seq study: MiAIRR



https://github.com/sfu-ireceptor/dataloading-curation

i∃ README.md

iReceptor Data Curation

This GIT repository contains example files and documentation for loading data into iReceptor repositories. Examples for metadata as well as rearrangement files for a number of widely used annotation tools are provided. The README files in each of the subfolders contain more documentation.

For more information on metadata curation, please refer to:

- The iReceptor Metadata documentation
- The iReceptor metadata example
- The AIRR repertoire metadata example

For more details on rearrangement curation, please refer to:

- The test data set documentation
- The AIRR rearrangement format (including igblast) example
- The MiXCR rearrangement format example
- The IMGT V-QUEST rearrangement example

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i∃ README.md

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	E C	F	0		I. I.	J	N	L	IVI	IN	0	P	Q
1	study_id	study_title	study_type	study_type_id	study_description	inclusion_exclusion_crit	grants	collected_by	lab_name	lab_address	submitted_by	pub_ids	keywords_study
2	PRJNA188191	Mining the antibody	Study	NCIT:C63536	HIV+ Study			pdkwong@nih.gov, ls	Kwong Lab	National Institute of Al	P.D. Kwong, J. Zhu	PMID: 23536288	contains_ig
3	PRJNA206548	Immunoglobulin ge	Case-Control Study	NCIT:C15197	Cancer Study			ramit.mehr@biu.ac.i	Ramit Mehr's Compu	Bar lian University	M. Michaeli, H. T	PMID: 24917868	contains_ig
4	PRJNA321261	Identification of shi	Case-Control Study	NCIT:C15197	Cancer Study	Inclusion breast cancer	Department of Defense	kapplerj@njhealth.o	Department of Immur	Department of Immund	D. J. Munson, C.A.	PMID: 27307436	contains_tcr
5	PRJNA312319	Tracking T-cell imm	Case-Control Study	NCIT:C15197	Cancer Study	HST transplant	Russian Science Four	chudakovdm@mail.r	Chudakov Lab Shemy	Russian Academy of Sc	I.V. Zvyagin, I.Z. N	PMID: 27811849	contains_tcr
6	PRJNA316033	T cell Beta chain rep	Study	NCIT:C63536	Cancer Study	Patients with esophagea	Natural Science Foun	keyang@bjmu.edu.cr	Key Laboratory of Car	Key Laboratory of Care	Z. Chen, C. Zhang,	PMID: 27171315	contains_tcr
7	PRJNA356992	Multi-omics study r	Study	NCIT:C63536	Cancer Study	primary liver carcinoma	National Key Researc	chengshj@263.net.cr	State Key Lab of Mole	National Cancer Centre	L. Shi, J. Wu, K. Zh	PMID: 28422742	contains_tcr
8	string	string	ontology	ontology	string	string	string	string	string	string	string	string	array
9	Unique ID assigned by study reg	Descriptive study ti	Type of study design	Type of study design (Ontol	Generic study descri	List of criteria for inclus	Funding agencies and	Full contact informat	Department of data c	Institution and institut	Full contact infor	Publications descr	Keywords describing

https://github.com/sfu-ireceptor/dataloading-curation

The iReceptor Data Curation process

The iReceptor team follows a relatively strict data curation process. This process is documented on the iReceptor Curation page. We do not discuss this process in detail here, but instead suggest simple processes that can make data curation easier to manage.

The iReceptor curation process is focused around the curation of data for a single study. As such, we recommend that all data that is being curated for a specific study be stored in a single directory. As an example, we will use one of the IMGT example data sets.

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Need help? Email us: support@ireceptor.org kira_neller@sfu.ca

Issue

Why is this a problem?

Issue	Why is this a problem?
Not providing annotations in an AIRR TSV format (or a format that can be converted to AIRR TSV).	Non AIRR-compliant data cannot be loaded into an ADC repository. Some repository data loaders (e.g. iReceptor Turnkey) accept other annotation tool formats (MiXCR, IMGT Vquest, igblast/AIRR TSV).

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Only providing processed sequences (e.g. CDR3s), not raw sequences	Hinders data re-use and verification

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Using incorrect formatting for miAIRR fields in metadata file	You shall not pass! The data loader will not load your data. Be mindful of different formatting types (string, ontology, integer, controlled vocabulary, boolean,)

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Not including all data processing details (tools and versions, QC/filtering steps, reference genomes, etc.)	Hinders data re-use and verification

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Not using the same subject/sample identifiers as in the published paper	Others cannot (easily) compare the dataset to the paper

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Not including all data processing details (tools and versions, QC/filtering steps, reference genomes, etc.)	Hinders data re-use and verification
Not using the same subject/sample identifiers as in the published paper	Others cannot (easily) compare the dataset to the paper
Not providing all available metadata	Though your study may not have considered certain variables (e.g. age), others may need these for data re-use

Part III: AIRR Data Commons Tool Demos

VDJServer Analysis Portal



TECHNOLOGY REPORT published: 08 May 2018 doi: 10.3389/fimmu.2018.00976



VDJServer: A Cloud-Based Analysis Portal and Data Commons for Immune Repertoire Sequences and Rearrangements

- NIAID-recommended service for immune repertoire analysis (R01 AI097403)
- Web browser interface: <u>https://vdjserver.org</u>
- Free Account
- Provides Immcantation tool suite and other specialized analysis tools
- MiAIRR study metadata entry
- Immune repertoire analysis
 - Pre-processing and quality control
 - Pre-processing visualizations
 - V(D)J gene assignment
 - Repertoire characterization and comparison
 - Analysis visualizations
- Community Data Portal
- Tool Ecosystem

Workflow Overview: What type of read level data do you have?



- Users can publish their studies making the data, metadata, analyses and visualizations available to the public.
 - Users can privately share project with other VDJServer users.
 - Users can publicly share by publishing to the Community Data Portal.
 - Not necessary to run analyses on VDJServer in order to share data.
- Sharing data can be as easy as 1, 2, 3:
 - 1. Create project
 - 2. Upload files to project
 - 3. Publish project

- VDJServer is a data repository in the AIRR Data Commons
 - 20+ studies, 2.5B rearrangement records
 - ADC API: https://vdjserver.org/airr/v1
 - Almost all studies are processed from SRA/ENA raw read data with VDJServer's analysis pipeline for consistency.
- VDJServer V2 brings new capabilities
 - MiAIRR data entry (AIRR Repertoire metadata) for studies
 - Integrated with iReceptor Plus platform
 - Users can perform comparative analysis between their private data and data queried from the AIRR Data Commons
 - Tracking the draft AIRR standards
 - Clones, trees, single cell, data processing, germline gene sets

- Publish study in the AIRR Data Commons with VDJServer
 - Additional steps beyond publishing to the AIRR Community Data Portal
 - Data needs to be compliant with AIRR Standards
 - VDJServer V1 projects require conversion
 - VDJServer V2 projects will be compliant automatically
 - Data needs to be processed through VDJServer's analysis pipeline.

- Based upon the size of the data, publishing can take hours or days
 - VDJServer admin performs the database load
 - Contact us to publish your study: vdjserver@utsouthwestern.edu

• Video demo: https://youtu.be/DgqKP-L75CM

Useful References

- Websites
 - AIRR Community: <u>www.airr-community.org</u>
 - iReceptor Website: www.ireceptor.org
 - iReceptor Scientific Gateway: gateway.ireceptor.org
 - VDJServer: https://vdjserver.org/
 - iReceptor Plus: <u>www.ireceptorplus.org</u>
- GitHub
 - https://github.com/sfu-ireceptor
 - https://github.com/airr-community
- Publications
 - iReceptor paper: Immunological Reviews (DOI: 10.1111/imr.12666)
 - AIRR Community paper: Frontiers in Immunology (DOI: 10.3389/fimmu.2017.01418)
 - AIRR Data Standards paper: Nature Immunology (DOI: 10.1038/ni.3873)
 - AIRR Data Rep paper: Frontiers in Immunology (DOI: 10.3389/fimmu.2018.02206)

Who to contact, How to Access

- AIRR Community:
 - Contact: <u>comm@airrc.antibodysociety.org</u>
 - AIRR Data Commons: https://www.antibodysociety.org/the-airr-community/airr-data-commons/
 - AIRR documentation: <u>http://docs.airr-community.org</u>
- iReceptor:
 - Contact: <u>support@ireceptor.org</u>
 - iReceptor Gateway account/access (<u>https://gateway.ireceptor.org</u>)
 - Download the iReceptor Turnkey repository (<u>https://github.com/sfu-ireceptor/turnkey-service-php</u>)
- VDJServer:
 - Contact: <u>vdjserver@utsouthwestern.edu</u>
 - VDJServer portal account: <u>https://vdjserver.org</u>

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 - iReceptor Plus: EU Horizon 2020 Research and Innovation Programme (#825821)
- Platform providers
 - Compute Canada
 - Texas Advanced Computing Centre