2023-08-14

Ontario Institute
for Cancer Research

Djerba: A Modular System to Generate Clinical Genome Interpretation Reports for Cancer

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OICR
Ontario Institute
for Cancer Research

Djerba

Introduction

1. Clinical reporting
2. How Djerba works
3. Going modular

github.com/oicr-gsi/djerba

1. Clinical Reporting

What is a clinical report?

- Report for an individual patient
- **Accredited** for clinical use
- Printable document:
  - Assay results
  - Interpretation
  - Treatment (if any)

Accreditation

CAP ACCREDITED
COLLEGE of AMERICAN PATHOLOGISTS

ACCREDITATION CANADA

CDC Centers for Disease Control and Prevention
CDC 24/7: Saving Lives, Protecting People™

Clinical Laboratory Improvement Amendments (CLIA)

OICR is the first lab in North America to be accredited with CAP, ACD and CLIA

Clinical Assays

Main assay

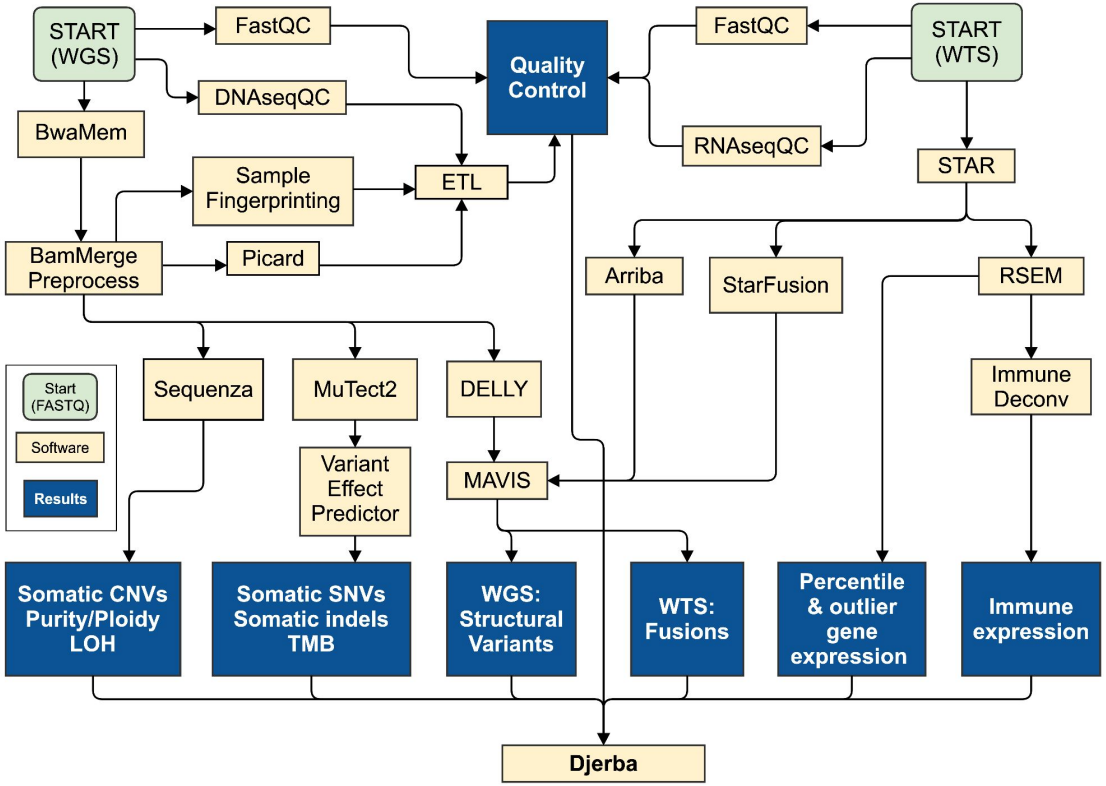
- Whole Genome and Transcriptome Sequencing: WGTS

Others

- Plasma Whole Genome Sequencing: PWGS

- Targeted Sequencing: TAR
- Whole Genome Sequencing: WGS

WGTS pipelines: From FASTQ to Clinical Report



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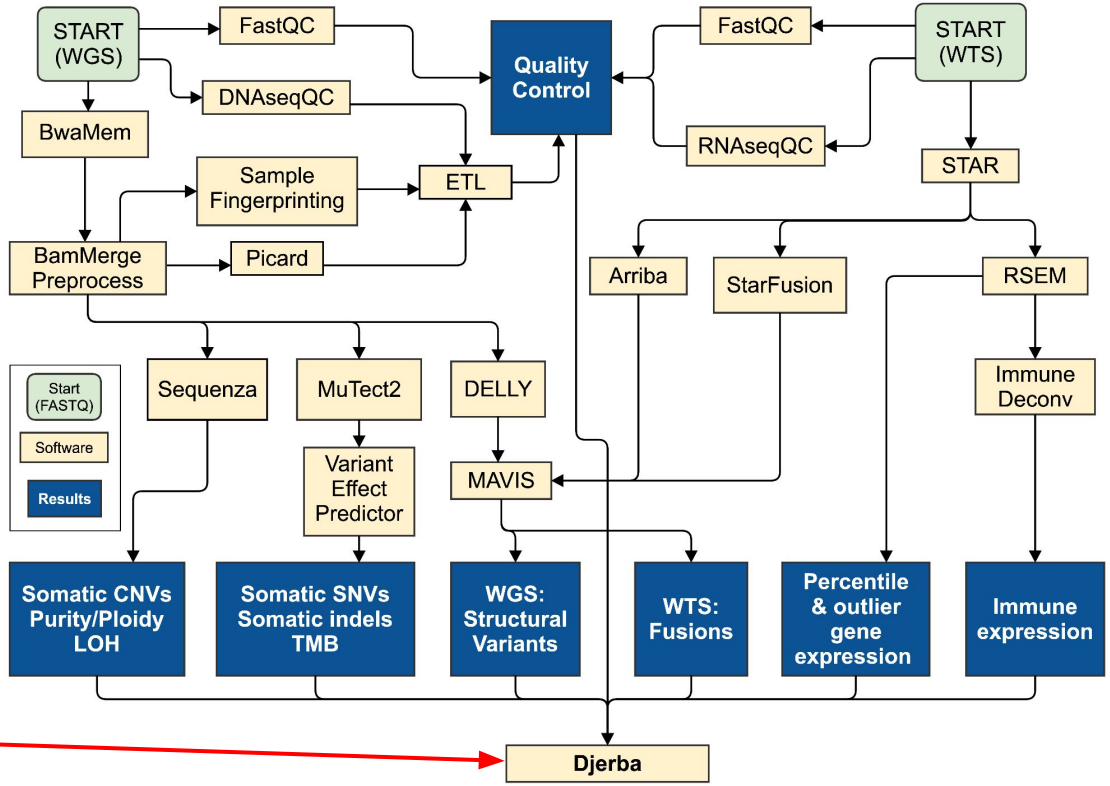
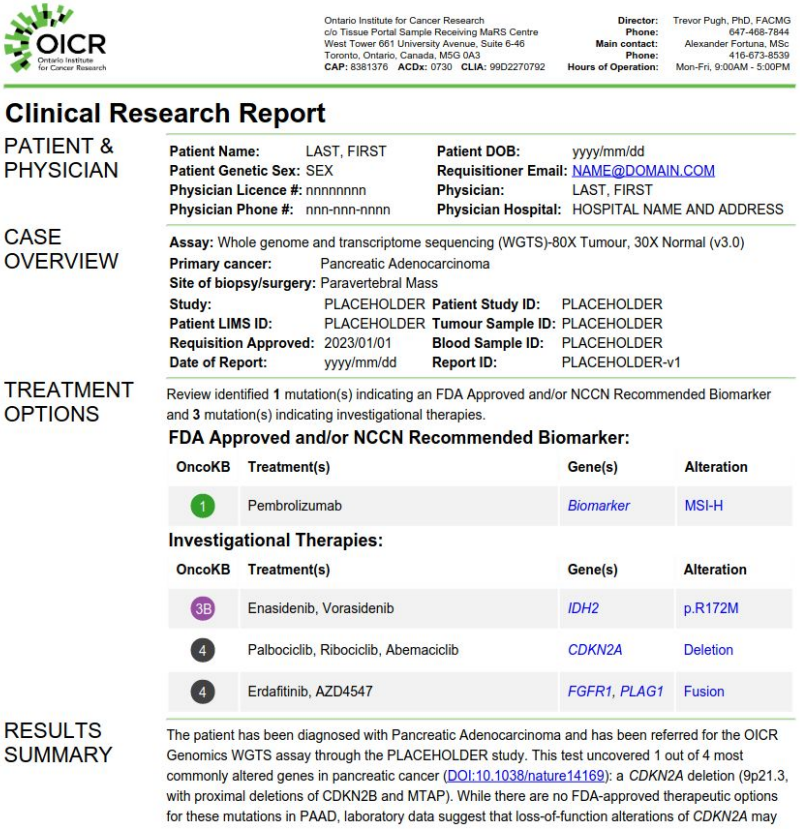


Collaborate. Translate. Change lives.

Clinical reporting: Example



Ontario Institute for Cancer Research
c/o Tissue Portal Sample Receiving MaRS Centre
West Tower 661 University Avenue, Suite 6-46
Toronto, Ontario, Canada, M5G 0A3
CAP: 8381376 **ACDx:** 0730 **CLIA:** 99D2270792

Director: Trevor Pugh, PhD, FACMG
Phone: 647-468-7844
Main contact: Alexander Fortuna, MSc
Phone: 416-673-8539
Hours of Operation: Mon-Fri, 9:00AM - 5:00PM

Clinical Research Report

PATIENT & PHYSICIAN

Patient Name: LAST, FIRST
Patient DOB: yyyy/mm/dd
Patient Genetic Sex: SEX
Requisitioner Email: NAME@DOMAIN.COM
Physician Licence #: nnnnnnnn
Physician: LAST, FIRST
Physician Phone #: nnn-nnn-nnnn
Physician Hospital: HOSPITAL NAME AND ADDRESS

CASE OVERVIEW

Assay: Whole genome and transcriptome sequencing (WGTS)-80X Tumour, 30X Normal (v3.0)
Primary cancer: Pancreatic Adenocarcinoma
Site of biopsy/surgery: Paravertebral Mass
Study: PLACEHOLDER **Patient Study ID:** PLACEHOLDER
Patient LIMS ID: PLACEHOLDER **Tumour Sample ID:** PLACEHOLDER
Requisition Approved: 2023/01/01 **Blood Sample ID:** PLACEHOLDER
Date of Report: yyyy/mm/dd **Report ID:** PLACEHOLDER-v1

TREATMENT OPTIONS

Review identified **1** mutation(s) indicating an FDA Approved and/or NCCN Recommended Biomarker and **3** mutation(s) indicating investigational therapies.

FDA Approved and/or NCCN Recommended Biomarker:

OncoKB	Treatment(s)	Gene(s)	Alteration
1	Pembrolizumab	*Biomarker*	MSI-H

Investigational Therapies:

OncoKB	Treatment(s)	Gene(s)	Alteration
3B	Enasidenib, Vorasidenib	*IDH2*	p.R172M
4	Palbociclib, Ribociclib, Abemaciclib	*CDKN2A*	Deletion
4	Erdafitinib, AZD4547	*FGFR1, PLAG1*	Fusion

RESULTS SUMMARY

The patient has been diagnosed with Pancreatic Adenocarcinoma and has been referred for the OICR Genomics WGTS assay through the PLACEHOLDER study. This test uncovered 1 out of 4 most commonly altered genes in pancreatic cancer (DOI:10.1038/nature14169): a *CDKN2A* deletion (9p21.3, with proximal deletions of CDKN2B and MTAP). While there are no FDA-approved therapeutic options for these mutations in PAAD, laboratory data suggest that loss-of-function alterations of *CDKN2A* may

Clinical reporting: Example

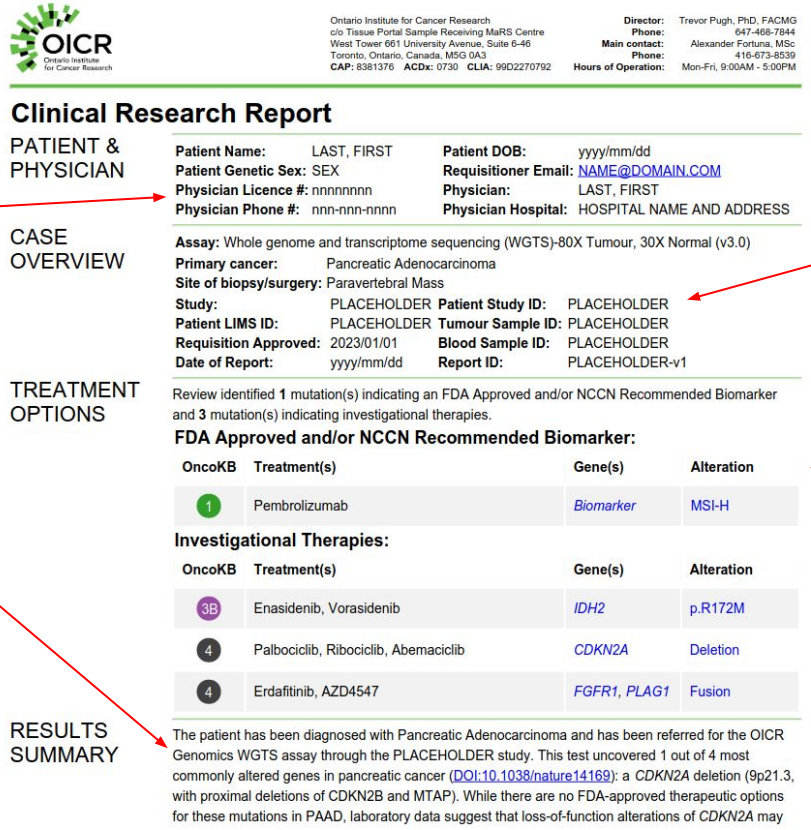
Patient metadata

Sample info

Therapies

Summary text

… and much more!



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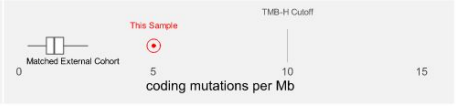
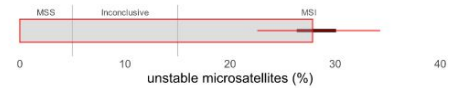
Clinical Reporting: Continued Example

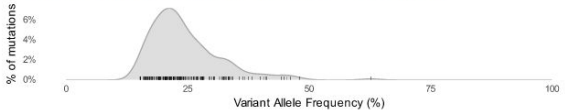
GENOMIC LANDSCAPE

Tumour Mutation Burden (TMB) was **5.02** coding mutations per Mb (187 mutations) which corresponded to the 71st percentile of the pan-cancer cohort and classifies it as **Tumour Mutational Burden Low (TMB-L, < 10 coding mutations / Mb)**. This TMB places the tumour in the **99th** percentile of the COMPASS cohort. The microsatellite status is **Microsatellite Instability High (MSI-H)**. This tumour has **55,699** candidate SNVs for ctDNA screening, making the sample **eligible** for OICR's plasma WGS assay (minimum of 4,000 SNVs required).

Biomarker	Call	Score & Confidence
TMB	TMB-L	
MSI	MSI-H	

SNVS AND IN/DELS

247 somatic mutation(s) were detected in exonic or splice regions, of which **187** impacted a coding sequence, and **2** corresponded to an oncogenic mutation, as defined by OncoKB.



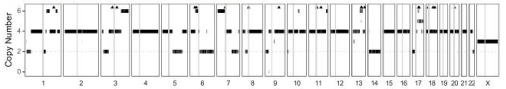
Gene	Chr.	Protein	Type	VAF	Depth	Expr. (%)	Copy State	OncoKB
IDH2	15q26.1	p.R172M	Missense Mutation	21	40/188	89	Neutral	3B
ZFHX3	16q22.2-q22.3	p.G1319Kfs*28	Frame Shift Ins	23	14/60	5	Neutral	N2

Chr.: Chromosome and cytoband

Expr. (%): Expression Percentile for gene mRNA, or NA if comparison data is not available

COPY NUMBER VARIATION

The percent genome altered (PGA) was **30%**. **9** cancer gene(s) were subject to copy number variation, of which **4** corresponded to an oncogenic alteration, as defined by OncoKB. Regions with large copy number gains (≥ 6 CN) marked as ▲ in plot below.



Gene	Chromosome	Expr. (%)	Alteration	OncoKB
CDKN2A	9p21.3	24	Deletion	4
CDKN2B	9p21.3	9	Deletion	N1
HMGA1	6p21.31	100	Amplification	N2
MTAP	9p21.3	4	Deletion	N2

Expr. (%): Expression Percentile for gene mRNA, or NA if comparison data is not available

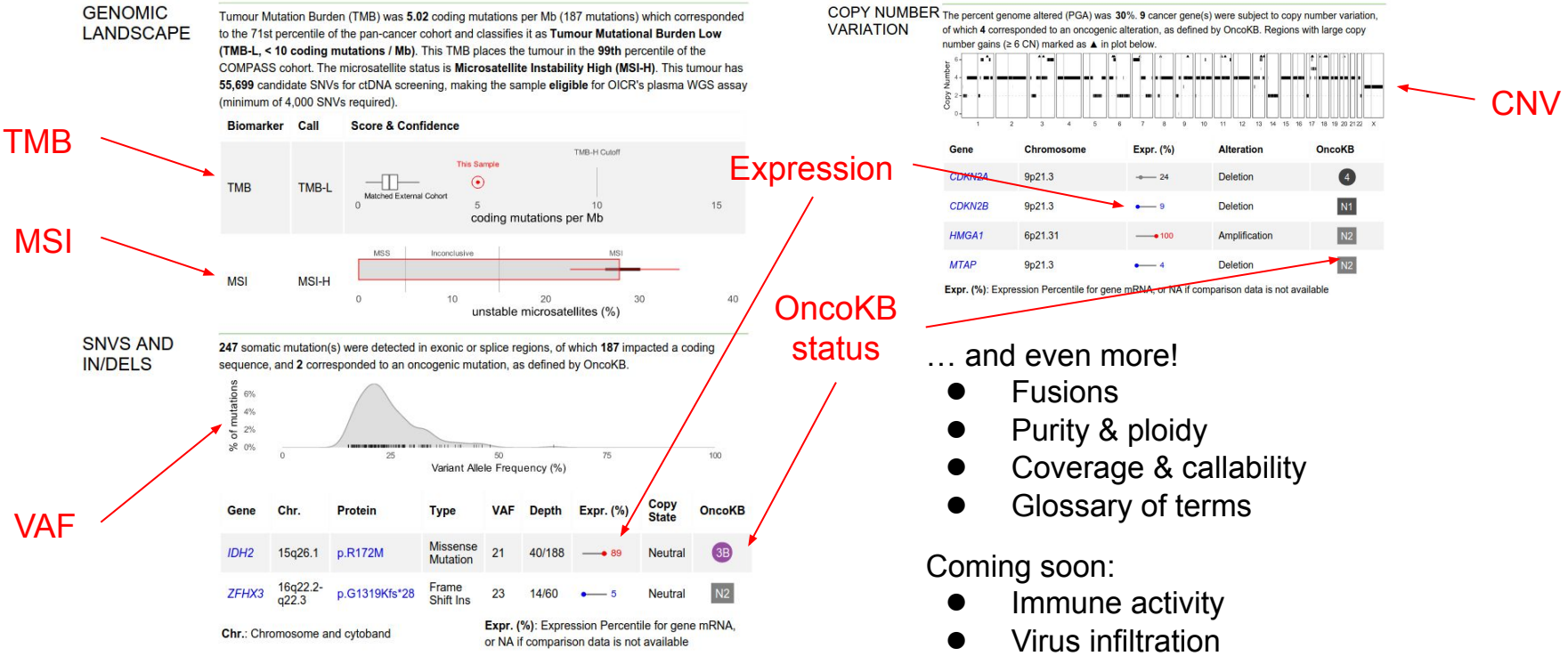
… and even more!

- Fusions
- Purity & ploidy
- Coverage & callability
- Glossary of terms

Coming soon:

- Immune activity
- Virus infiltration
- Tissue of origin inference

Clinical Reporting: Continued Example



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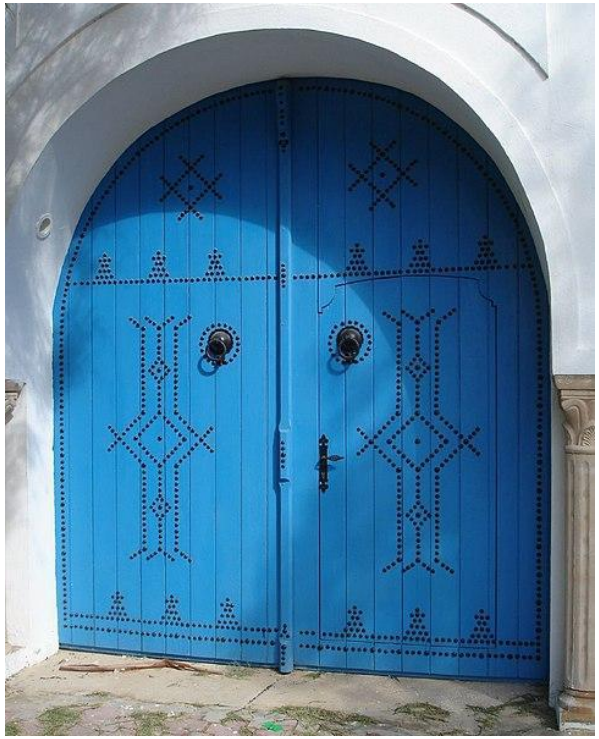
2. How Djerba works

Introducing Djerba

- `github.com/oicr-gsi/djerba`
- Developed from scratch
- No existing application filled its niche
- Open source
- GPL 3.0 licence
- 100+ reports since January 2022



Doorway on the island of Djerba
Photo by Alain Feulvarch, Wikimedia Commons

How Djerba works

Step	Format	Read by
Configure	INI	Human 😀
Extract	JSON	Machine 🤖
Render	HTML	Human 😀
Publish	PDF	Human 😀

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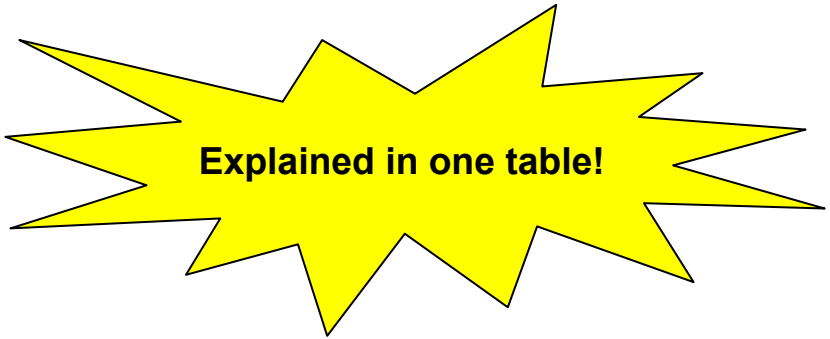
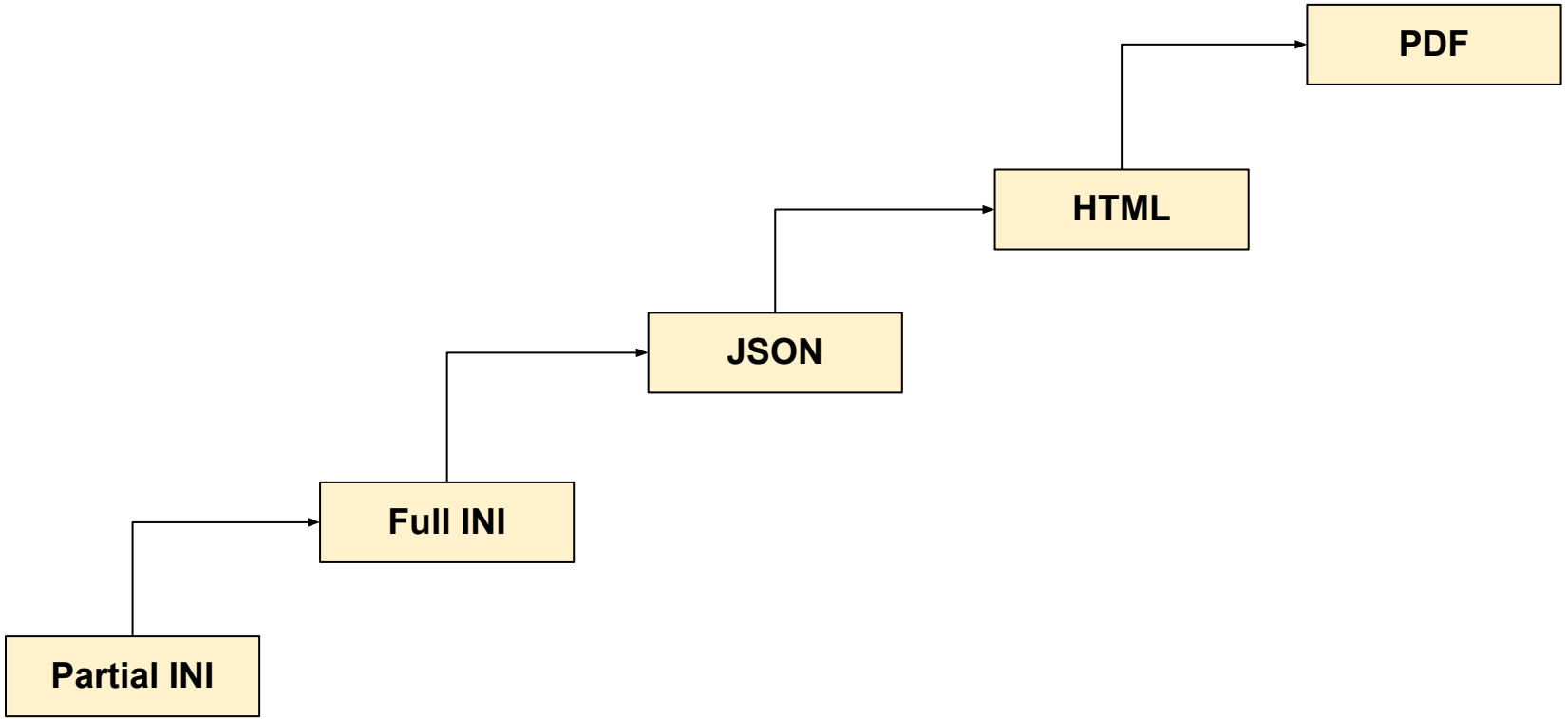
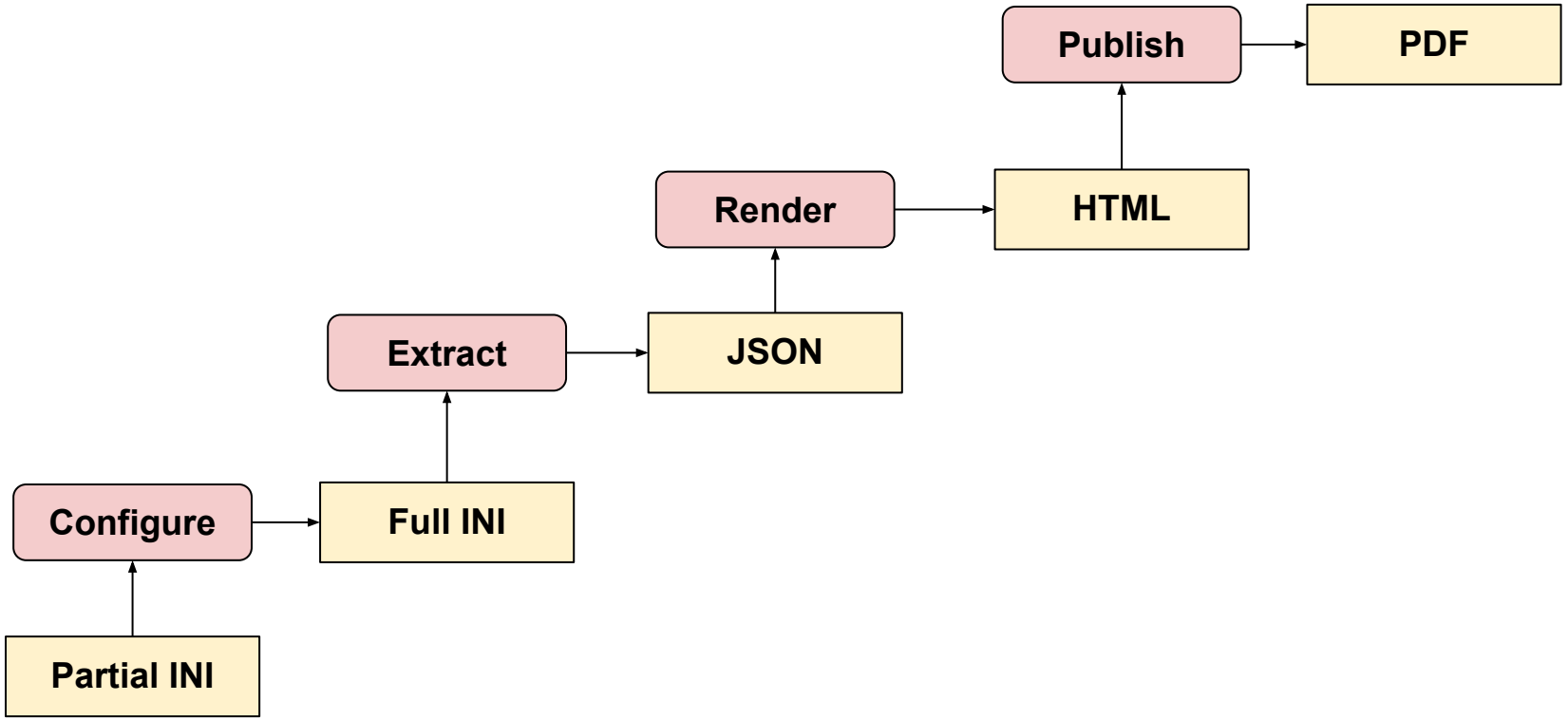


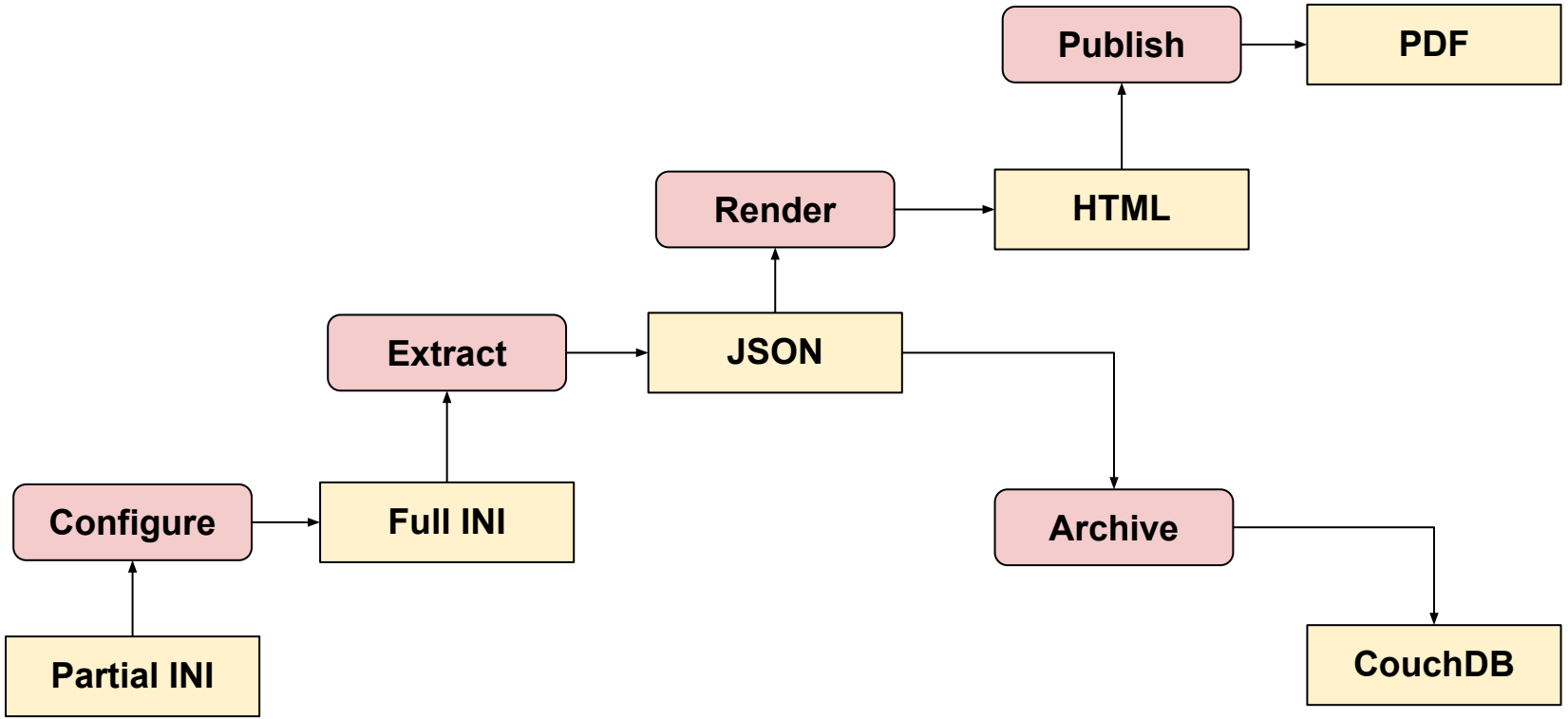
Djerba steps: File types



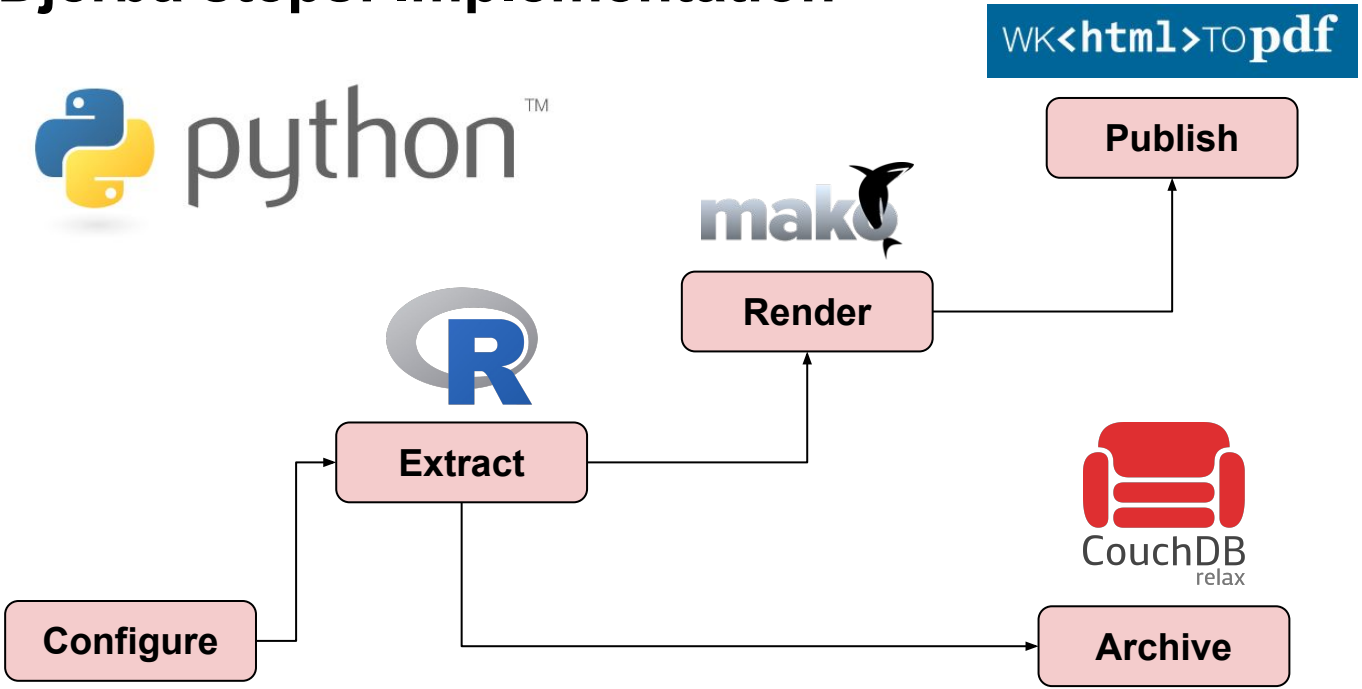
Djerba steps: File types and actions



Djerba steps: File types and actions and more!

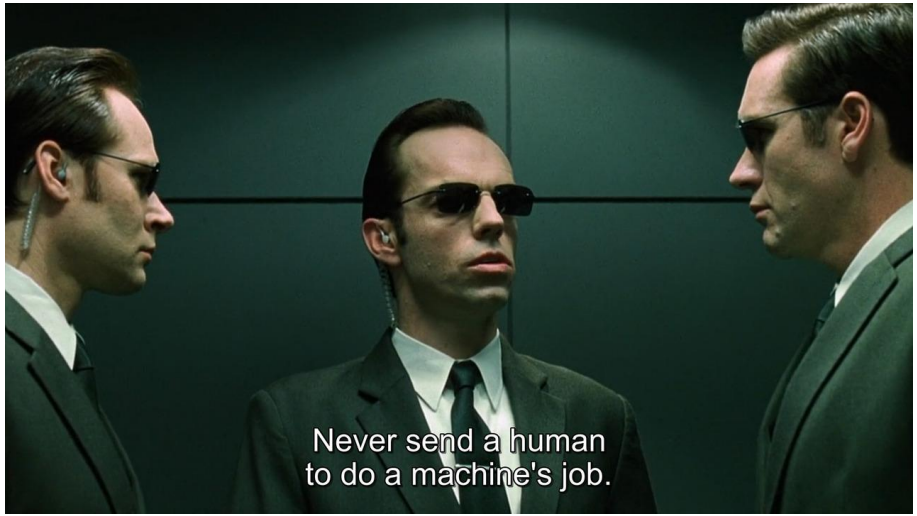


Djerba steps: Implementation



Running Djerba

```
djerba.py report --ini config.ini --out ./output
```



3. Going modular

Collaborate. Translate. Change lives.

Plugins for Djerba

- Djerba is growing
- Make it modular!
- **Core** manages the plugins
- **Plugins** are easy to:
  - Write
  - Test
  - Update
  - Share

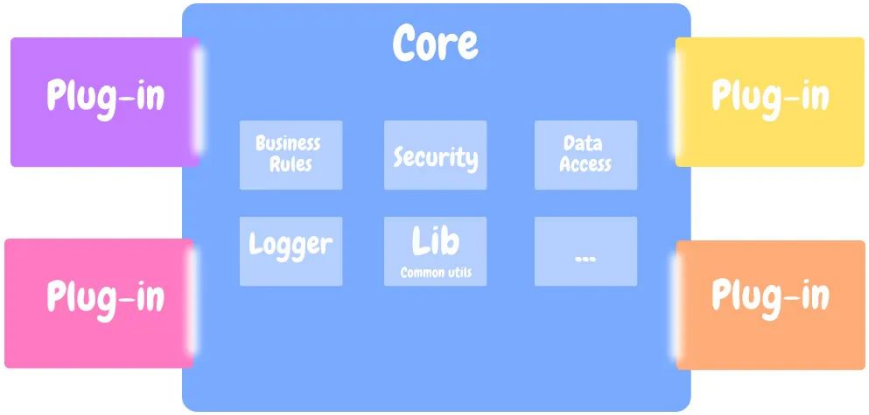


Image via https://medium.com/omarelgabrys-blog

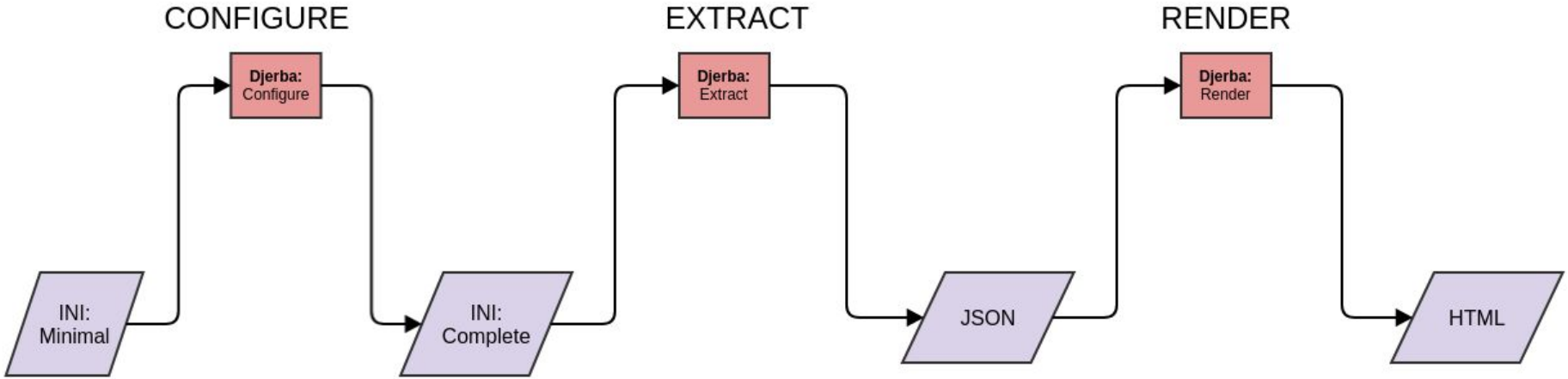
Complex interconnected system

Simple plugins in a well-defined framework

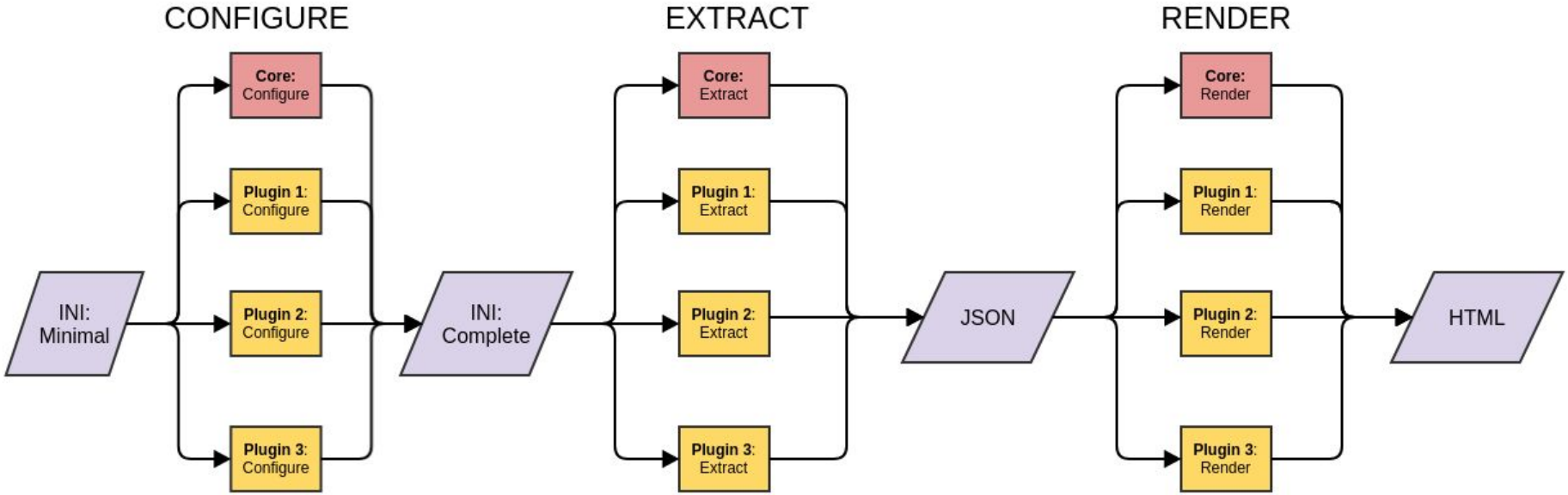
Plugins are Miniature Djerbas

- Generate a **section** of the report
  - Configure INI
  - Extract JSON
  - Render HTML
- The Djerba **core**:
  - Runs multiple plugins
  - Makes the completed report
- Launch September 2023

Reminder: Djerba without plugins



New and improved: Djerba with plugins



Collaborate. Translate. Change lives.

Plugin capabilities

- Generate example INI files
- Required and default parameters
- Runtime priorities
- Shared workspace
- Merge outputs
- … and more!

Conclusion

Summary

- Djerba is a system for clinical reports
- 4 steps:
  - Configure INI
  - Extract JSON
  - Render HTML
  - Publish PDF
- JSON archived to CouchDB database
- Modular structure enables extension and collaboration
- Github: `oicr-gsi/djerba`

Acknowledgements

- Alex Fortuna
- Felix Beaudry
- Aqsa Alam

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is provided by the Government of Ontario