

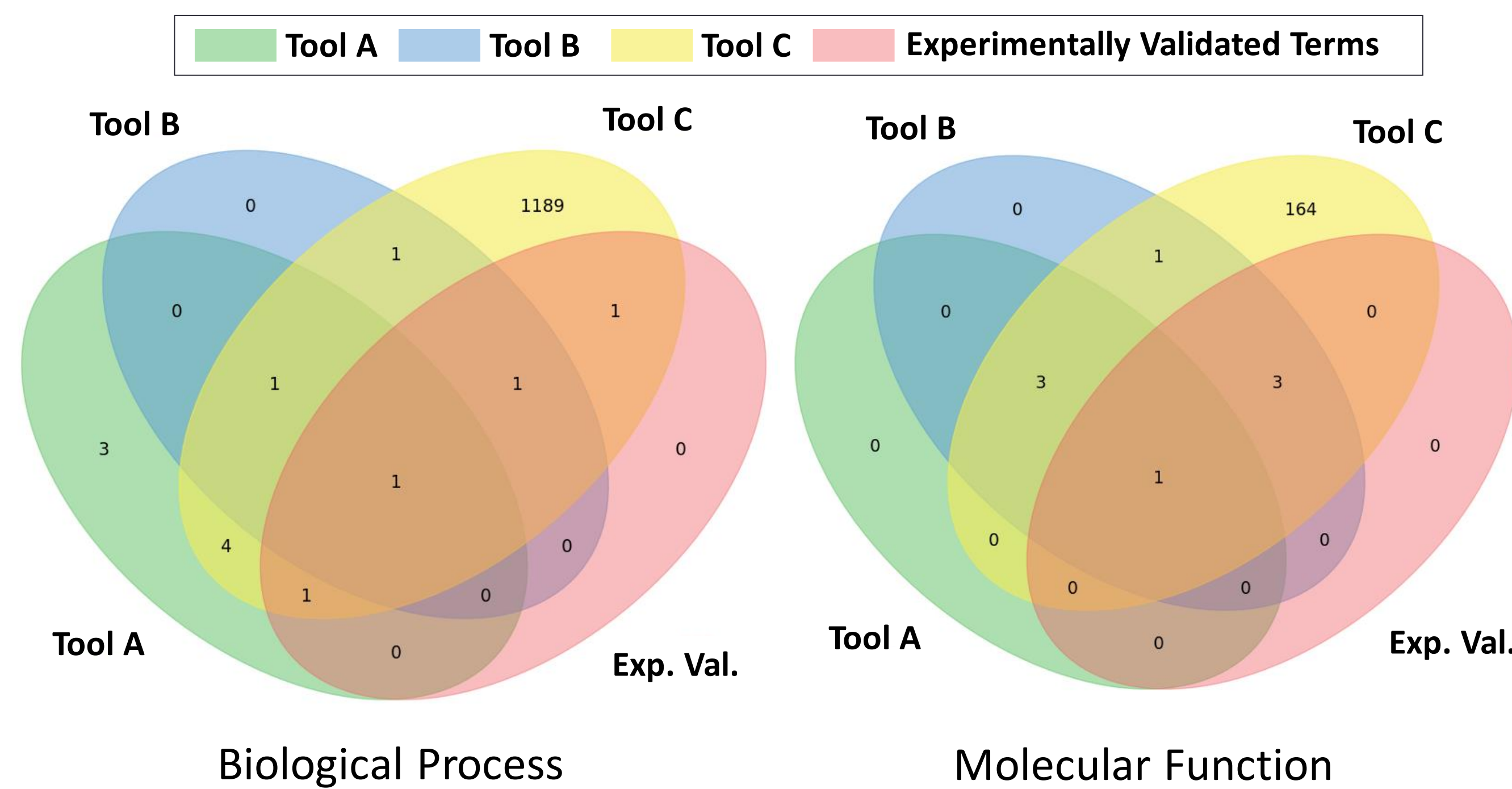
A Look Back at the Quality of Protein Function Prediction Tools in CAFA

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PROTEIN FUNCTION PREDICTION

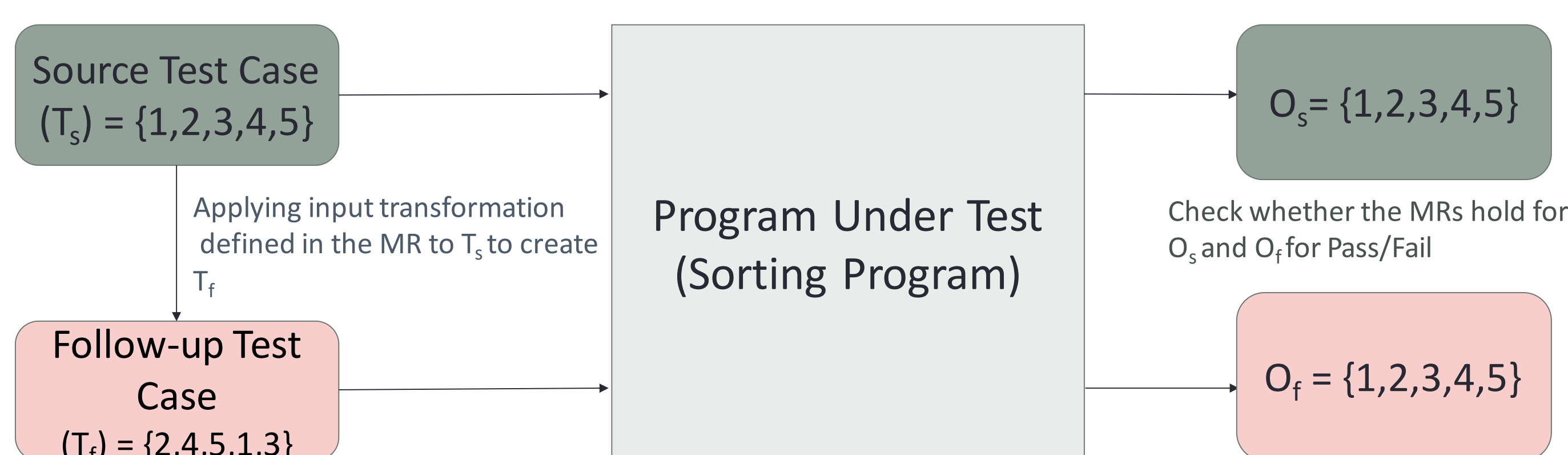
- Automated Function Prediction (AFP) tools will play a very important role in medicine and health care in the future.
- However, current tools predict different sets of Gene Ontology (GO) terms for the same input and only few terms are common with the experimentally validated terms.
- Experimentally validated terms are assumed incomplete.
- Consequently, biologists and developers will find difficulty in selecting and testing a tool, respectively.



GO terms for Tyrosinase (TYRO_HUMAN)

METAMORPHIC TESTING

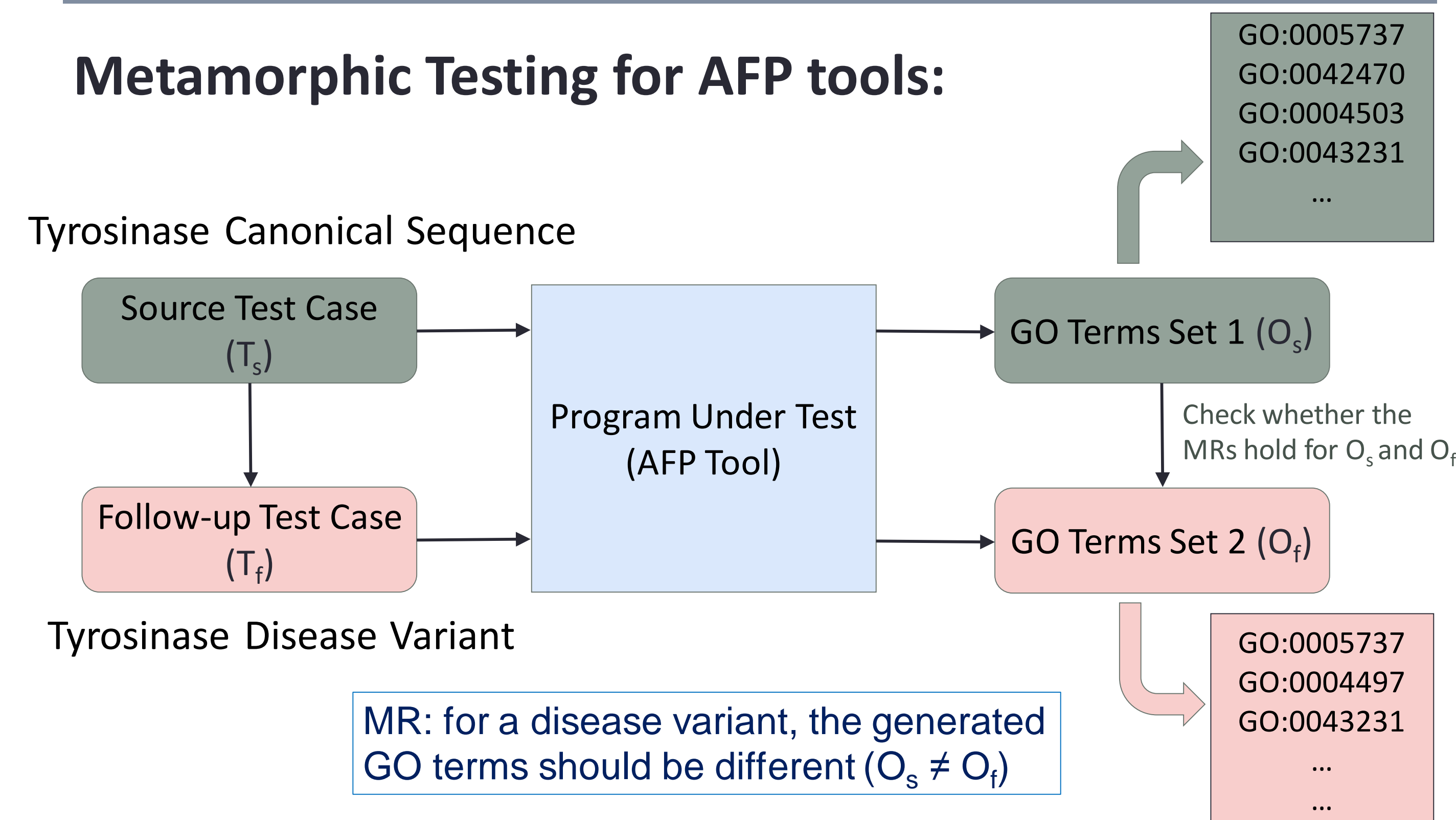
- A technique used to test programs for which the correct output is unknown or practically difficult to determine.
- checks whether the program behaves according to an expected set of properties: metamorphic relations (MRs).
- Specifies how a particular change to the input of the program should change the output.
- MR is violated when the change in output differs from the definition.



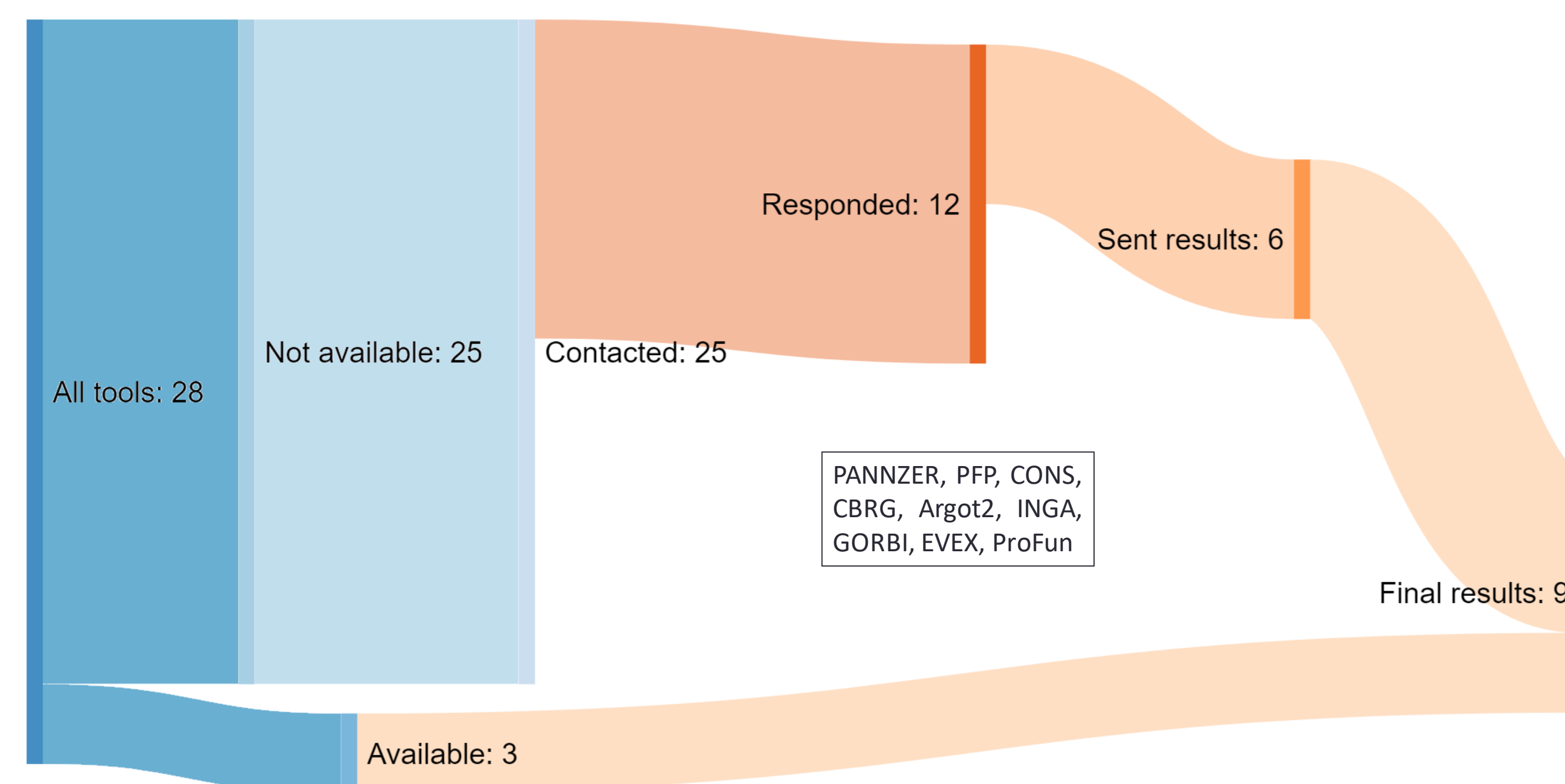
MR: output should be equal for a permuted input ($O_s = O_f$)

METHODOLOGY

Metamorphic Testing for AFP tools:



Tools: CAFA top-performers

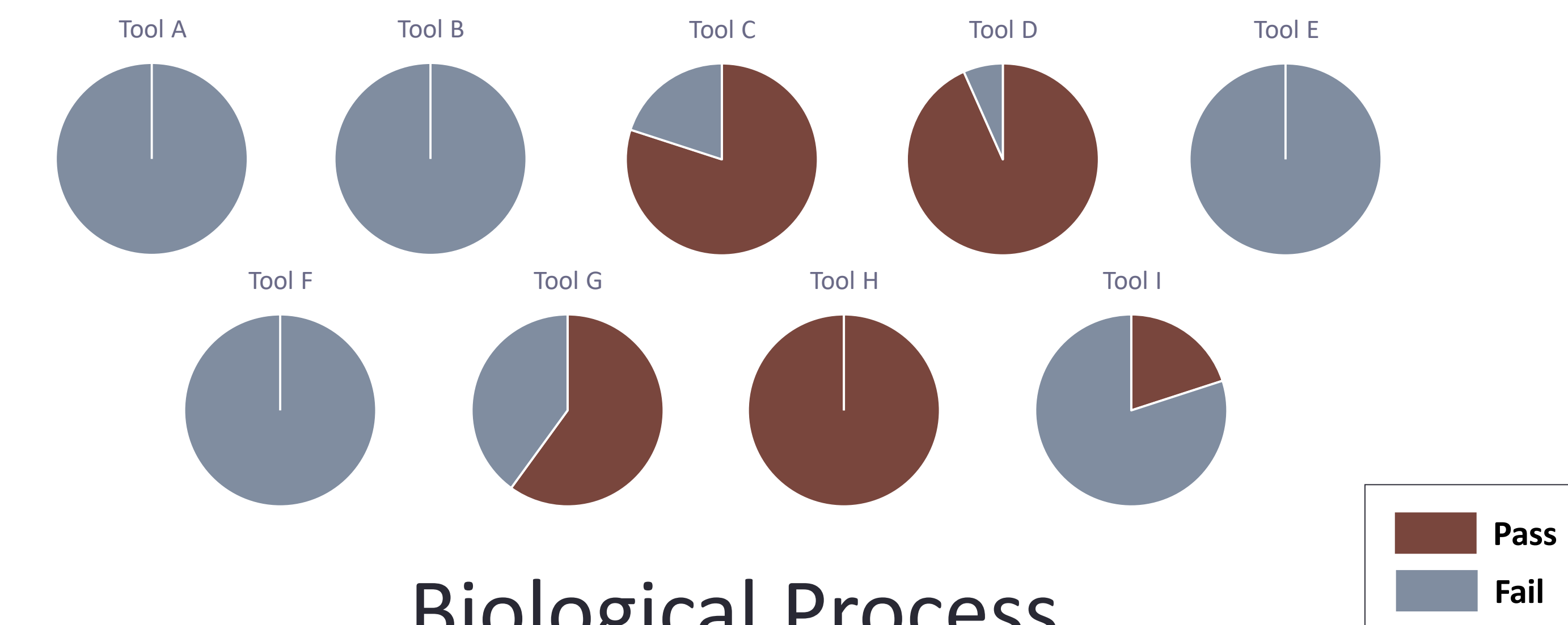


Data: Carefully selected proteins and their variants

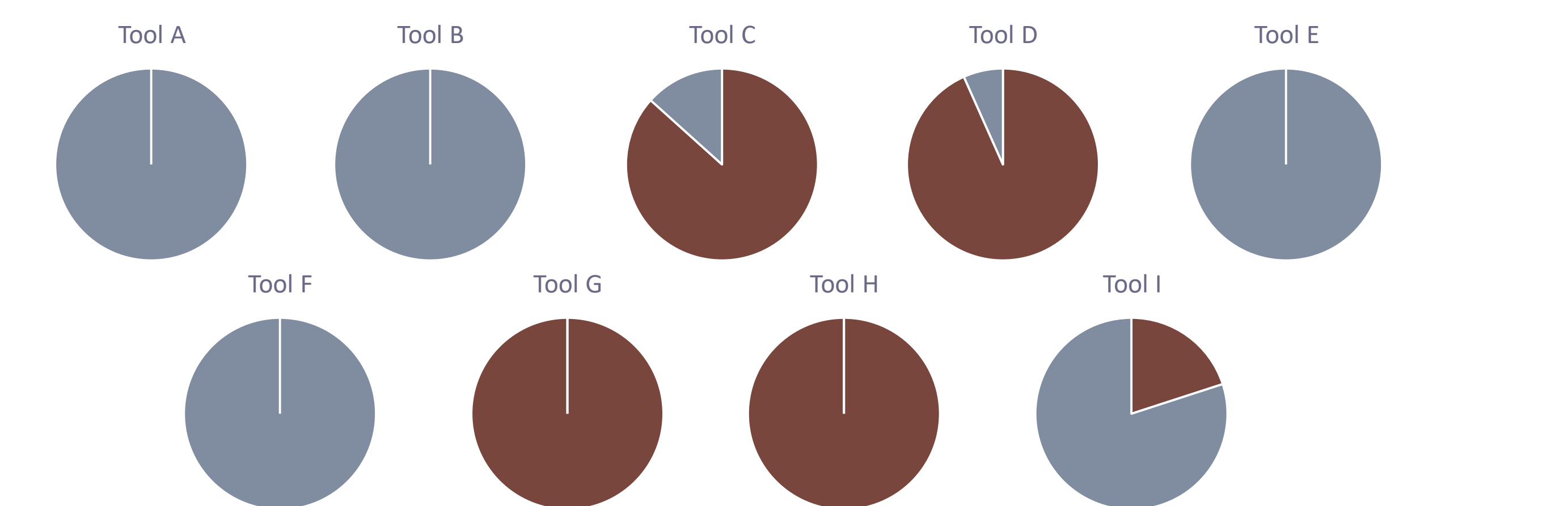
Protein	Source test case	Follow-up test cases
Tyrosinase (TYRO_HUMAN)	Canonical sequence	7 Disease Variants (Albinism)
Cytokine receptor common subunit gamma (IL2RG_HUMAN)	Canonical sequence	4 Disease Variants (severe combined immunodeficiency)
Toll-like receptor 4 (TLR4_HUMAN)	Canonical sequence	2 Natural Variants 2 Splice Variants (soluble decoy receptors)

RESULTS

Molecular Function



Biological Process



CONCLUSIONS

- Possible to create MRs based on carefully selected protein examples.
- Many tools did not pass all test-cases.
- AFP community need to work together for QA of AFP tools.
- MT seems to be a promising avenue for testing AFP tools.

FUTURE WORK

- Communicate results to authors and post-analysis.
- Explore more specific MRs: "is there a change?" vs. "actual change".
- Develop an expanded test-suite:
 - Explore the feasibility of developing MRs for *Cellular Component*.
 - Different types of test-cases, different species.
 - Testcases/MRs for HPO term prediction.
- Work with the AFP community to expand the number of tested tools.
- Develop a MT testing framework readily available to users.

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