

# Swiss Variant Interpretation Platform for Oncology (SVIP-O)

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In 2015, the Clinical Bioinformatics group of the [Swiss Institute of Bioinformatics](#) (SIB) launched a working group for somatic mutation calling, in order to harmonise and improve practices of next-generation sequencing (NGS) in cancer diagnostics and foster a community in molecular pathology, oncology, and haemato-oncology across Swiss hospitals. The group comprises medical and computational experts from all university hospitals and other medical institutions. Because cancer is caused by changes (also called variants) in the genes of diseased cells, molecular variants represent the source code of the disease. Genomic analysis of tumours using NGS has become a standard practice in Swiss hospitals to support diagnosis and treatment decisions. Certain drugs target cancer cells with very specific variant fingerprints and, therefore, certain variants can cause a drug to be less efficient or even detrimental. Thus, a properly annotated and interpreted meaning for a variant across several cancer types is important for treatment decisions.

A key insight from the working group was the absence of a harmonised, central repository of clinically verified variants in patients. Harmonisation is critical to enable different institutions with their own in-house tools to compare results and ideally share previously found evidence between them. Subsequently, diagnosis will also be harmonised, ensuring that it depends entirely on the tumour and not the hospital visited.

The suggestion of centralising somatic variants in one single platform, harmonising their annotation, mutually agreeing on their clinical interpretation, and using SIB resources to support the curation of previously undescribed variants has been accepted as an infrastructure development project as part of the national [Swiss Personalized Health Network](#) (SPHN) initiative.

The Swiss Variant Interpretation Platform (SVIP) will provide a joint knowledge-base for somatic variants found in Swiss hospitals during cancer diagnostic sequencing (see [figure 1](#)). Submission of new variants will be batch based and coupled with the retrieval of database snapshots capturing annotations and interpretations for the given set of variants. This will be further enriched with an API enabling seamless integration into existing pathology information systems. SVIP will incorporate variant informa-

tion from other similar projects such as ClinVar, ClinGen, CIViC, OncoKB, and PMKB, to facilitate the prioritisation of variants by molecular pathologists. These projects are very similar to SVIP in what they are doing, but each is optimised for its local legal and ethical framework. However, SVIP also aims to enable pathologists and oncologists to check whether a variant has been seen in another institution in Switzerland, and subsequently contact the colleague to discuss potential treatment.

In an initial ramp up, SVIP will reconcile previous somatic variants of the partner hospitals to provide a harmonised annotation. In addition to increasing the frequency of some rare variants, this step will make it possible to identify conflicting annotations in partnering institutions. Discrepancies will then be resolved by a clinical expert panel. The panel will also validate new annotations generated by the SVIP curation team, based on public evidence (e.g., curated databases, literature). Finally, SVIP will offer a finely customisable notification framework that can inform medical institutions on changes in annotation of earlier submissions.

SVIP is an ambitious project to establish a Swiss one-stop shop for the interpretation of somatic variants, enabling faster and more robust prioritisation. A high-quality, joint variant annotation pipeline will ensure reproducibility and consistent data stewardship. The secure interpretation transaction space for molecular pathologists and oncologists will make it possible to establish a continuous learning system, contributing to improved interpretation of variants also globally. In the near future, the SVIP platform will extend to include germline variants. Unlike somatic variants, which are specific to a particular neoplastic process, germline mutations express patient specific characteristics, which may play a role in the treatment of cancers as well as in several other diseases or syndromes.

## Disclosures

No potential conflict of interest relevant to this article was reported.

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**Figure 1:** SVIP will leverage routine data from daily clinical work to improve cancer diagnostics, by making annotation parsimonious across all treating institutions in Switzerland and having national experts jointly agree on a common interpretation of patients' variants. Furthermore, by having all variants jointly annotated in one place, more variants can reach meaningful levels of frequency than any single hospital could achieve on its own.

