Whole Framome Vaccination against tumor neoantigens

With fast sequencing of tumor DNA, several years ago, came the possibility to discover neoantigens, expressed by the tumor but not by healthy cells. The entire immuno-oncology industry has based neoantigen discovery on whole exome sequencing (i.e. sequencing of 1% of the cancer genome). In combination with checkpoint inhibitors, which take the brake off the immune system, this opens the option of personalized vaccination of a patient against her/his own cancer. While preclinical experiments seemed promising, clinical trials showed underwehelming effects thus far.

Frame combines Whole Genome Sequencing with a combination of long range RNA sequencing (Oxford Nanopore) plus short read RNA sequencing, and developed a proprietary bioinformatics pipeline. With this we identify what we call the Framome, that is the complete set of neo open reading frames expressed by the tumor as result of mutations. Most of those mutations, e.g. Structural Variations, abundant in most common cancers, have been missed by exome sequencing.

Using this approach we design vaccines that instead of 10 neoantigenic amino acids, as used before, encode up to a 100 times more, 1000 neoantigenic amino acids, similar to foreign viruses. We developed a procedure to go from one thin needle tumor biopsy to Framome vaccine design in two weeks. In preclinical experiments these Framome vaccines seem powerful, and they are now ready for clinical testing.