Methods: A systematic search of coding MS and FSDN in LS tumors published in literature and in public databases was performed (Seltar Database; The Cancer Genome Atlas, TCGA), with application of epitope prediction pipelines and prioritization of FSDN with the greatest coverage on the most frequent HLA-I and HLA-II haplotypes (pVACbind; pVACtools v2.0.1).

Results: 531 frame-shift peptide sequences derived from -1 (m1) and -2 (m2) nucleotide deletions from 269 coding microsatellites (cMS) of at least 8 bases were retrieved from SelTarbase and TCGA. Data in FASTA format was computed through the pVACbind epitope prediction pipeline with a labile HLA-binding affinity threshold (IC50 $= <$ 5000 nM) to consider immunoediting events. We prioritized 98 epitopes, 53 HLA-I and 45 HLA-II restricted, from an original predicted number of 42828 HLA-I and 8350 HLA-II-restricted (m1 and m2) epitopes with a median coverage of 9,4 HLA-I alleles and 8,7 HLA-II alleles per epitope.

Conclusions: Our predicted neoepitope set has an optimal coverage among LS patients in terms of HLA alleles, associated cancers and prevalence. These results are key to first perform ex vivo functional analysis to determine neoepitopes immunogenicity to later design a preventive antitumoral vaccine for LS.

Legal entity responsible for the study: The authors.

Funding: FIS PI19/01867, funded by Instituto de Salud Carlos III.

Disclosure: All authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2021.05.050

SO-26 In-silico Lynch syndrome-related neoantigens prediction for a dendritic cell-based cancer prevention vaccine

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Background: Lynch syndrome (LS), caused by germline mutations in DNA mismatch-repair genes (MLH1, MSH2, MSH6, PMS2) predisposes patients to colorectal and endometrial cancer (CRC, EC), among other tumors. Although CCR prevention methods are effective, no preventive strategies exist for the majority of LS-related tumors. Ex-vivo generated and tumor-antigen-loaded dendritic cell (DC) vaccines are one of the recently featured antitumoral immunotherapies. However, their full therapeutic potential would likely be as a preventive approach in high-risk cancer patients. LS is a paradigmatic model for its limited and predictive mutational spectrum in repetitive DNA sequences termed microsatellites (MS). This study aims to identify the main frame-shift derived neopeptides (FSDN) that are shared among cancers from LS patients with the purpose of developing a DC-based neoepitope vaccine.