### Exercises Monday 25th April Personlig Medicin Master PART 2

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Variant not found - GLP-1 R

What happens when you don't find your variant of interest?

As an example, we are going to work with a variant in glucagon-like peptide-1 receptor to assess wheter patients bearing that mutation can respond to Ozempic

This is our sequence:

>Human glucagon-like peptide-1 receptor mRNA (Patient X)

TTCCGCAGGTGGCAGCGATGGCCCAGTCCTGAACTCCCCGCCATGGCCGGCGCCCCCGGCCCGCTGCGCC

TTGCCGTGCTGCTGCTCGGGATGGTGGGCAGGGCCGGCCCCCGCCCCCAGGGTGCCACTGTGTCCCTCTG

GGAGACGGTGCAGAAATGGCGAGAATACCGACGCCAGTGCCAGCGCTCCCTGACTGAGGATCCACCTCCT

GCCACAGACTTGTTCTGCAACCGGACCTTCGATGAATACGCCTGCTGGCCAGATGGGGAGCCAGGCTCGT

TCGTGAATGTCAGCTGCCCCTGGTACCTGCCCTGGGCCAGCAGTGTGCCGCAGGGCCACGTGTACCGGTT

CTGCACAGCTGAAGGCCTCTGGCTGCAGAAGGACAACTCCAGCCTGCCCTGGAGGGACTTGTCGGAGTGC

GAGGAGTCCAAGCGAGGGGAGAGAAGCTGGGGGGAGGAGCAGCTCCTGTTCCTCTACATCATCTACACGG

TGGCGTACGCACTCTCCTTCTCTGCTCTGGTTATCGCCTCTGCGATCCTCCTCGGCTTCAGACACCTGCA

CTGCACCAGGAACTACATCCACCTGAACCTGTTTGCATCCTTCATCCTGCGAGCATTGTCCGTCTTCATC

AAGGACGCAGCCCTGAAGTGGATGTATAGCACAGCCGCCCAGCAGCACCAGTGGGATGGGCTCCTCTCCT

ACCAGGACTCTCTGAGCTGCCGCCTGGTGTTTCTGCTCATGCAGTACTGTGTGGCGGCCAATTACTACTG

GCTCTTGGTGGAGGGCGTGTACCTGTACACACTGCTGGCCTTCTCGGTCTTCTCTGAGCAATGGATCTTC

AGGCTCTACGTGAGCATAGGCTGGGGTGTTCCCCTGCTGTTTGTTGTCCCCTGGGGCATTGTCAAGATCC

TCTATGAGGACGAGGGCTGCTGGACCAGGAACTCCAACATGAACTACTGGCTCATTATCCGGCTGCCCAT

TCTCTTTGCCATTGGGGTGAACTTCCTCATCTTTGTTCGGGTCATCTGCATCGTGGTATCCAAACTGAAG

GCCAATCTCATGTGCAAGACAGACATCAAATGCAGACTTGCCAAGTCCACGCGGACACTCATCCCCCTGC

TGGGGACTCATGAGGTCATCTTTGCCTTTGTGATGGACGAGCACGCCCGGGGGACCCTGCGCTTCATCAA

GCTGTTTACAGAGCTCTCCTTCACCTCCTTCCAGGGGCTGATGGTGGCCATCTTATACTGCTTTGTCAAC

AATGAGGTCCAGCTGGAATTTCGGAAGAGCTGGGAGCGCTGGCGGCTTGAGCACTTGCACATCCAGAGGG

ACAGCAGCATGAAGCCCCTCAAGTGTCCCACCAGCAGCCTGAGCAGTGGAGCCACGGCGGGCAGCAGCAT

GTACACAGCCACTTGCCAGGCCTCCTGCAGCTGAGACTCCAGCGCCTGCCCTCCCTGGGGTCCTTGCTGC

AGGCCGGGTGGCAATCCAGGTGGGAGAGACACTCCCAGGGACAAGGGAAGGAAGGGACACACACACACAC

ACACACACACACACACACACACATACATCCTGCTTTCCCTCCCCAAACCCATCAGACAGGTAAATGGGCA

GTGCCTCCTGGGACCATGGACACATTTTCTCCTAGGAGAAGCAGCCTCCTAATTTGATCACAGTGGCGAG

AGGAGAGGAAAAACGATCGCTGTGAAAATGAGGAGGATTGCTTCTTGTGAAACCACAGGCCCTTGGGGTT

CCCCCAGACAGAGCCGCAAATCAACCCCAGACTCAAACTCAAGGTCAACGGCTTATTAGTGAAACTGGGG

CTTGCAAGAGGAGGTGGTTCTGAAAGTGGCTCTTCTAACCTCAGCCAAACACAGAGCGGGAGTGACGGGA

GCCTCCTCTGCTTGCATCACTTGGGGTCACCACCCTCCCCTGTCTTCTCTCAAAGGGAAGCTGTTTGTGT

GTCTGGGTTGCTTATTTCCCTCATCTTGCCCCCTCATCTCACTGCCCAGTTTCTTTTTGAGGGCTTGTTG

GCCACTGCCAGCAGCTGTTTCTGGAAATGGCTGTAGGTGGTGTTGAGAAAGAATGAGCATTGAGACACGG

TGCTCGCTTCTCCTCCAGGTATTTGAGTTGTTTTGGTGCCTGCCTCTGCCATGCCCAGAGAATCAGGGCA

GGCTTGCCACCGGGGAACCCAGCCCTGGGGTATGAGCTGCCAAGTCTATTTTAAAGACGCTCAAGAATCC

TCTGGGGTTCATCTAGGGACACGTTAGGAATGTCCAGACTGTGGGTGTAGGTTACCTGCCACTTCCAGGA

CGCAGAGGGCCAAGAGAGACATTGCCTCCACCTCTCCTGAATACTTATCTGTGACCACACGCTGTCTCTT

GAGATTTGGATACACTCTCTAGCTTTAGGGGACCATGAAGAGACTCTCTTAGGAAACCAATAGTCCCCAT

CAGCACCATGGAGGCAGGCTCCCCCTGCCTTTGAAATTCCCCCACTTGGGAGCTGATATACTTCACTCAC

TTTTCTTTATTGCTGTGATAGTCTGTGTGCACAATGGGCAATTCTGACTTCTCCCATCTAGTGGAAATGA

GCGAAATCATGGTTGTAGTGATCTTG

1. Where is the position of the variant and what is the change compared to the reference genome?
2. Is the mutation translated into a change in the protein product?
3. Is the mutation known?
4. Can we predict the effects of the mutation? Consider the following points:
   1. Is the change in the amino acid a disruptive change?
   2. Is the mutation located in a particular protein domain?
   3. Is the mutation in the transmembrane region? or in the GLP-1 binding region?
   4. Will the mutation prevent the interaction with agonist peptides?
   5. Will the mutation affect the interaction with other relevant proteins?
   6. Do you expect that the mutation will generate a different protein structure?
5. Based on the above analysis. Do we expect that Ozempic will bind to GLP-1 R in this patient?