

Tentamen GCA 2014 (12 jan 2015)

Short answers are preferred. Please notice that the questions are on molecular processes and therefore the answer should involve the (biochemical)molecular details.

- 1) Describe the experiment that already in 1928 demonstrated that DNA must be the carrier of heritable information. (50)
- 2) Explain in no more than 50 words how strand discrimination occurs in mismatch correction in mammalian cells. (Use most recent literature) (50)
- 3) During proof reading by the DNApolIII enzyme a mis-incorporated base can be removed by the exo-nucleolytic activity of the enzyme. How does the enzyme 'know' when a base should be removed. (50)
- 4) Describe in no more than seven lines the function of the CSB protein in TCR based on recent literature. (50)
- 5) The SIR2 protein in yeast (and probably SIRT1 in mammalian cells) links chromatin organization and metabolism. Explain the biochemistry of this link. (50)
- 6) Lysine deacetylation and Lys9 methylation are both important processes in gene-silencing and genome organization. Explain how both these processes, once started, spread. What are the similarities between both mechanisms for spreading of gene-silencing? (75)
- 7) Describe the experimental evidence that lysine9 methylation might take its cue (is initiated by) from deacetylation. Similarly, describe the evidence that DNA methylation might take its cue from histone H3 Lys9 methylation. (75)
- 8) Describe in no more than ten lines the principle of Chip-Seq (not the deep sequencing part!). Describe in no more ten lines the principles of MethylC-Seq en BS-seq (not the deep sequencing part!) (50)
- 9) Describe the experimental evidence that cytosine methylation in non CpG sequences (so-called CHG and CHH sequences) might be characteristic for the embryonic status of stem cells. (50)
- 10) Explain how the Hitchinson-Gilfort (HGPS) associated mutations in the *LaminA/C* gene lead to the production of the so-called $\Delta 50$ version of LaminA. What might be the effect of the presence of this LaminA $\Delta 50$ protein? (75)
- 11) Does the paper by Agrelo et al. (Agrelo R et al. JCO 2005;23:3940-3947) proof that:
 - *LaminA/C plays a role in hematologic malignancies?
 - *hypermethylation of LaminA/C is the cause hematologic malignancies?Answer these questions in a few lines that explain your answers. (50)