

Bioingeniørutdanningen

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1. The title of the project

"Mechanisms of action of IL1 in the brain and mechanisms of fever and/or depression"

2. Background and research question

IL1 is a proinflammatory cytokine that attracted the attention of neuroscientist because of the changes in brain functions at the beginning of inflammatory diseases or infections by Gram negative bacteria. The observed sleepiness of infected subjects was first studied in Pappenheimer' lab. Later the role of IL1 in development of sickness feeling was widely studied. Sickness feeling symptoms are similar to symptoms of major depression. IL1 plays a role in the onset and maintenance of these symptoms. It also turned out that IL1 has a role in development of fever via activation of COX-2. A molecular cascade behind IL1R connects COX-2 to the IL1R. The molecular mechanisms of fever are initiated by the NFkB gene transcription regulator.

The warm sensitive cells of the brainstem controlling body temperature regulation are involved in fever mechanism. The thesis will describe the body temperature regulation system from textbook to review articles. Then it will show the IL1 receptor distribution in the brain and we will discuss the IL1 sources in the brain at the level of review papers. We will give a brief survey about the molecular network of IL1R from the receptor to gene transcription and interpret its action on cell metabolism. Then we will turn to depression and show the analogous symptoms of depression and sickness feeling. Finally, we will try to compose a common molecular network controls fever, sickness feeling and depression.

3. Materials and Methods

The thesis will be written as a review-article using the IMRAD method. An electronic database search of PubMed and Web of Science with several keywords will be performed. These will include IL1, IL1R, depression, fever, COX-2, sickness feeling and NFkB gene transcription regulator. We will mainly use review articles on the selected topics to write the thesis. We also might use references used in the review articles and do additive literature database searches.

4. Ethical considerations

This study is based on other articles and research, and therefore we expect that these are ethically performed.

5. Progress plan

Week 14

- Hand in the project plan.
- The first guidance of the process from Turid Aarhus Braseth.
- Search for references.
- Guidance from Gabor Juhász and Alvhild Alette Bjørkum will happen after we hand in the project plan and thesis sections (IMRAD-sections) week by week during the whole Bachelor period.

Week 15

- Start writing the introduction part of the thesis.

Week 16

- Continue writing the introduction
- The second guidance of the process from Turid Aarhus Braseth.

Week 17

- Continue writing the introduction.

Week 18

- Write the result, discussion and conclusion part of the thesis.
- Midway presentation on the 28th of April.

Week 19

- Continue writing the result, discussion and conclusion.
- Start writing the abstract and method.

Week 20

- Finalise the thesis and hand in the first draft.
- The third guidance of the process from Turid Aarhus Braseth.

Week 21

- Make corrections to the thesis.

Week 22

- Hand in the thesis on the 29th of May.

Week 23

- The poster will be made, and the oral examination of the thesis will be completed.

Week 24

- Oral examination on the 9th or 10th of June.

6. Resources

The thesis will be written by students at the Faculty of Engineering and Natural Sciences at Western Norway University of Applied Sciences in collaboration with Eötvös Loránd University in Budapest, Hungary. We are working with Gabor Juhász at the Faculty of Science at Eötvös Loránd University and Alvhild Alette Bjørkum at the Faculty of Engineering and Natural Sciences at Western Norway University of Applied Sciences. The resources required for writing the thesis are the databases PubMed and Web of Science.

7. References

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- Lawrence, T. (2009). The nuclear factor NF-kappaB pathway in inflammation. *Cold Spring Harbor perspectives in biology*, *1*(6), a001651-a001651. doi:10.1101/cshperspect.a001651
- Pasic, C. J., Levy, D. W., & Sullivan, D. M. (2003). Cytokines in Depression and Heart Failure. *Psychosomatic Medicine*, 65(2), 181-193. doi:10.1097/01.PSY.0000058372.50240.38
- Roerink, M. E., van der Schaaf, M. E., Dinarello, C. A., Knoop, H., & van der Meer, J. W. (2017). Interleukin-1 as a mediator of fatigue in disease: a narrative review. *J Neuroinflammation*, *14*(1), 16. doi:10.1186/s12974-017-0796-7