The authors have engaged in an important study attempting to understand the gene expression in two areas of the brain on different periods of bacterial meningitis utilizing a well established animal model. The hypothesis is sound: gene activation will be different in the hypocampus than in other parts of the brain in addition to this expression being temporary related. Trying to understand gene expressions interactions rather than the consequence to the single gene expression is a contemporary approach to grasp the complexity of this disease process. The ability to understand the implications of these gene to gene interactions on different times and further more the ability to interfere in this process is the future.

The authors have engaged in a first attempt to conceptualize an interaction that equates more likely to a non linear dynamics rather than a linear process. Focusing on microglia, the primary cells responsible of inflammation, and neuronal stem cells, the primary cells responsible of reparation is also a well based mechanistic approach. The methodology includes data mining, data dimension reduction and other interpretations which the reader may not be familiar with, however when we attempt to understand this complex pathways of inflammation, defense and regeneration, the simple method of linear dynamics is inapplicable.

The authors were able to reproduce, as they have done before, severe bacterial meningitis in this animal model. The authors were able to find temporal/related activation of gene in infected animals and the lack of it in the control animals. They were also able to find a substantial difference in the inflammatory activation of the hypocampus where a more significant apoptotic damage was found. More interestingly they found a significant amount of down regulated genes that lead to similar development and differentiation of the hypocampus at 24 hours. This is a “peak hole” view of future treatment. Neurogenesis, axogenesis and synaptogenesis have now a time and a location where future therapies should be geared.

As the authors describe the complexity of the similar networks interaction forces us to interpret the findings with caution, however the biological relevance of these findings provides an opportunity to start investigating specific tailored therapies.
As we have learned from our colleagues from Hematology/Oncology, in the approach of many individuals with cancer there are different faces. The same principals should apply to bring injury processes, in particular those that are initiated by infections or inflammatory events. There is a period in which the infections should be overcome followed in which a period of the inflammation should be modulated which straddles with the period of which a component of stimulation is needed for regeneration to occur. However the regeneration does not guarantee function as the crucial period of integration of new neurons through synamptogenesis is essential most likely followed by a period of pruning to decrease excessive irritability that can lead to inadequate regulation of neurons with excessive metabolic demands and indiscriminated liberation of neural transmitters.

I applaud the authors effort in courageously taking the endeavor of taking the “eagle’s view” of the gene expression during meningitis. I am looking forward to see their observations once they attempt to interact with this immune regulative networks to modulate inflammation and direct neuronal repair mechanisms.

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Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.