**P38 MAPK, A Potential Therapeutic Target for Multiple Sclerosis Treatment**

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**Multiple Sclerosis (MS)**

<table>
<thead>
<tr>
<th>MS Types</th>
<th>MS Causes</th>
<th>MS Symptoms</th>
<th>MS Pathology</th>
<th>Treatments</th>
<th>Directions</th>
</tr>
</thead>
</table>
| Relapsing-remitting MS | Unknown       | Fatigue, Fatigue, Cognitive impairment, Depression, Unstable mood | Inflammation is a hallmark of MS, and P38 MAPK plays a role in regulating inflammatory responses. | Disease-modifying agents:  
- Teriflunomide  
- Interferon-1α  
- Interferon-1β  
- Glatiramer acetate  
- fingolimod  
- Mitoxantrone  
- Dimethyl fumarate  
- Natalizumab | No available disease-modifying agents  
Only medications that help to manage the symptoms |
| Progressive MS     | Risk factors  | Venous: Hemorrhagic, Optic neuritis, Diabetic, Speech: Dysarthria   | Blood-brain barrier disturbance is a significant feature of MS, and P38 MAPK involvement has been reported. | Medication that help to manage the symptoms |

**Introduction - P38 MAPK**

The p38 mitogen-activated protein kinase (MAPK) family is important in response to extracellular signals, expressed ubiquitously throughout the body. It consists of four isoforms: p38α, p38β, p38γ, and p38δ.

**Results - P38γ in Myelination**

P38γ knockout mouse brains show earlier myelination in the corpus callosum, and other white matter areas (data not shown).

**Future Directions**

- P38γ-deficient mouse brains show earlier myelination.
- P38γ expression is low during active myelination of the brain.
- P38γ mRNA level is also up-regulated in white matter lesion of MS patients.
- P38γ might be an inhibitor of oligodendrocyte differentiation and/or myelination and also possibly blocking remyelination in MS patients.

**Conclusion**

- P38γ-deficient mouse brains show earlier myelination.
- P38γ expression is low during active myelination of the brain.
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**Inflammation**

- Genetics: Mutation in genes involved in the human leukocyte antigen (HLA) system, located on chromosome 6.
- Geography: Sun exposure is inversely related to the risk for MS development.
- Infections: Infected by certain viruses, such as Epstein-Barr virus and others, can raise the risk of developing MS.  

**MS Symptoms**

- **Fatigue**
- **Cognitive impairment**
- **Depression**
- **Unstable mood**

**MS Pathology**

- **Inflammation**: In the relapsing-remitting stage of MS, initial tissue injury is associated with CD8+ T cells and/or activation of resident microglia attacking myelin which is made by oligodendrocytes. Invasion of T cells, B cells and macrophage through damaged blood-brain barrier causes further myelin deconstruction.
- **Blood-brain barrier (BBB) disturbance**: A profound damage to the BBB is caused by initial inflammation. BBB rupture is also observed in progressive MS, but its correlation with inflammation is not well understood.
- **Plaques**: Completely demyelinated regions, demyelinated axons that are embedded in astrocitoc scar tissue, and massive loss of axons appear as plaques.

**MS Causes**

- Unknown
- Risk factors

**MS Types**

- Relapsing-remitting MS
- Progressive MS

**MS Symptoms**

- Venous: Hemorrhagic, Optic neuritis, Diabetic
- Speech: Dysarthria

**MS Pathology**

- Disease-modifying agents:
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  - Natalizumab

**Treatments**

- Medication that help to manage the symptoms

**Future Directions**

- No available disease-modifying agents
- Only medications that help to manage the symptoms

**Results - P38γ in Myelination**

Microarray data from Bruce Trapp lab

**Conclusion**

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