BIO_03 - Development and Characterization of Anti-VLA4 Monoclonal Antibody as a Potential Biopharmaceutical for the Treatment of Multiple Sclerosis

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Introduction: Multiple Sclerosis (MS) is an inflammatory neurodegenerative disease that affects almost 3 million people worldwide. Monoclonal antibodies (mAbs) such as Natalizumab have become an important pillar in MS treatment. It binds to α4β1 integrin (VLA4), which is crucial in mediating the transmigration of immune cells to inflammatory sites. However, since Natalizumab recognizes α4 subunit, that is also present in α4β7 integrin, it may cause side effects, such as Progressive Multifocal Leukoencephalopathy, an under-described serious adverse reaction commonly identified in JC virus-positive patients.

Objectives: The present work aimed to develop and characterize an IgG4 mAb against VLA4, and to compare its biological activity *in vitro* with Natalizumab.

Methodology: The anti-VLA4 mAb CDR was previously designed *in silico* and patented by our group. Light and heavy IgG chains were expressed in EXPI293F cells. The supernatant was collected and purified by affinity chromatography. The fractions were pooled desalted and concentrated. Purified anti-VLA4 mAb final lot was subjected to molecular characterization by different molecular approaches. Functional assays to evaluate mAb- VLA4 interaction included flow cytometry and transmigration assay using Jurkat cells and lymphocytes from heathy blood donnors.

Results: Anti-VLA4 mAb was successfully expressed and purified, yielding 25.2mg/L. Characterization assays showed it is appropriately folded in solution and close to the expected size of 150kDa. Flow cytometry interaction assay confirmed its specificity and binding capacity to VLA4. Accordingly, transmigration functional assays confirmed the biological activity by reducing Jurkat cells and human lymphocytes transmigration in 46% and 34%, respectively, comparing to untreated control. Natalizumab was used as positive control and showed reduction rate of 54% and 66%, respectively.

Conclusion: In summary, anti-VLA4 mAb was successfully obtained, with satisfactory yield and generated a functional and complete antibody. In addition, our data corroborate the hypothesis that the mAb can modulate VLA4-mediated transmigration of immune cells, confirming its potential as an applicable biotherapeutic in MS treatment.

Keywords: Multiple Sclerosis, Biotherapeutic, Monoclonal Antibodies