～LSC学術講演会のご案内～

メルボルン大学フローリー神経学研究所 Fazel Shabanpoor 氏の講演会を企画致しました。多数のご来聴をお待ちしております。

日時: 2016 年 10 月 31 日（月）14:00～15:00

教室: LSC カンファレンスルーム（神戸学院大学ポートアイランドキャンパス、C号館1階）

講師: Fazel Shabanpoor 氏／メルボルン大学フローリー神経学研究所・シニアリサーチオフィサー

演題: Identification of a blood-brain barrier penetrating peptide for systemic brain delivery of morpholino oligonuclotides

主催：戦略的研究基盤形成支援事業

講演要旨:

Identification of a blood-brain barrier penetrating peptide for systemic brain delivery of morpholino oligonuclotides

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Splice-switching antisense oligonucleotides (SSOs) are emerging as treatments for neuromuscular diseases, with several SSOs currently undergoing clinical trials. Recently eteplirsen (EXONDYS 51), an SSO based on morpholino chemistry targeting exon-51 skipping of dystrophy has been approved by FDA for treatment of Duchenne muscular dystrophy (DMD). However, therapeutic development of SSO has been hampered by poor cellular uptake and tissue penetration, including crossing of the blood-brain barrier (BBB) to reach targets in the central nervous system (CNS). For spinal muscular atrophy (SMA) application, we have investigated the ability of BBB-crossing peptides for CNS delivery of splice-switching phosphorodiamidate morpholino oligonucleotides (PMO) targeting survival motor neuron-2 (*SMN2*) exon 7 inclusion. We identified a branched derivative of the well-known ApoE (141-150) peptide, which as a PMO conjugate was capable of exon inclusion in the CNS following systemic administration, leading to the restoration of a full-length *SMN2* transcript. Treatment of newborn SMA mice with this peptide-PMO conjugate resulted in a significant increase in the average lifespan, increase in weight, muscle strength and righting reflexes. Treatment of adult SMA mice with this newly identified peptide-PMO also resulted in a significant increase in the level of SMN expression in the CNS. This work provides proof of principle for the ability to select new peptide paradigms to enhance CNS activity of a PMO. We hope further peptide sequence refinement will enable this new peptide-based delivery platform to be developed for CNS delivery of PMO SSOs for the treatment of neuromuscular and neurodegenerative diseases.