

## Advances in Nucleic Acid Medicine Delivery to the Brain

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**Abstract** - The phage display technology is widely used for identification and isolation of peptides that bind to a particular target with high affinity and specificity. Although a number of phage-derived peptides have been identified that bind to cerebral capillaries, conjugation of particulate drug delivery systems with such peptides have yielded disappointing results in brain targeting on intravenous injection [1]. To address these shortfalls, we introduced a phage mimetic termed NanoLigand Carriers (NLCs) to efficiently target and cross brain capillaries on intravenous injection [2]. NLCs are self-assemblies of a brain-specific phage display peptide conjugate that engage their targets through a hierarchical presentation of display peptides (e.g., as in protofilaments). On intravenous injection, NLCs reach the brain in substantial quantities without disrupting the integrity and functionality of the BBB. NLCs accommodate a wide range of guest molecules and targets two cellular receptors. On reaching the brain-parenchyma, NLCs carrying therapeutic nucleic acids engage with microglial cells and neurons, exerting unprecedented pharmacological effects without inducing inflammation and metabolic perturbations [2]. NLCs therefore overcome previous limitations in active targeting with particulate drug carriers, including those decorated with phage display peptides.

### References

- [1] SM Moghimi & ZS Farhangrazi (2020) Therapeutic Delivery 11:465.
- [2] L-P. Wu et al. (2019) Nature Communications 10:4635.