To: John H. Reynolds
Subject: Highlights

Date: September 2, 1986 From: P.M. Lippiello

1. Testing of potential new ligands for nicotine receptor binding studies continued. N-methyl cytisine was synthesized by Dr. Tomas Hudlicky (VPI) and forwarded to RJR for assessment of its potency in inhibition binding assays. This compound was found to be approximately 100-fold less effective in inhibiting [3H]-nicotine binding to rat brain tissue than its parent compound, cytisine, and 15-fold less potent than L-nicotine in doing so. Therefore, the N-methyl derivative does not appear to be suitable as a potential radioligand for nicotine receptor characterization. The synthesis of halogenated derivatives of cytisine will now be undertaken.

2. Repurification of L-[3H] nicotine, routinely utilized in nicotine receptor studies, became necessary because it was found that commercially available material contained 13-18 % radiochemical impurities.

3. Recent evidence in the literature, based on model cell systems, suggests that the turnover of membrane lipids and the activity of a phosphorylating enzyme system (protein kinase C) may be closely linked to nicotine receptor function in the peripheral nervous system. A pilot study is being planned, in collaboration with personnel in the Department of Biochemistry at BGSM, to determine whether a similar link exists in the brain.