

## SP-SAP : How It's Different From Substance P Antagonists

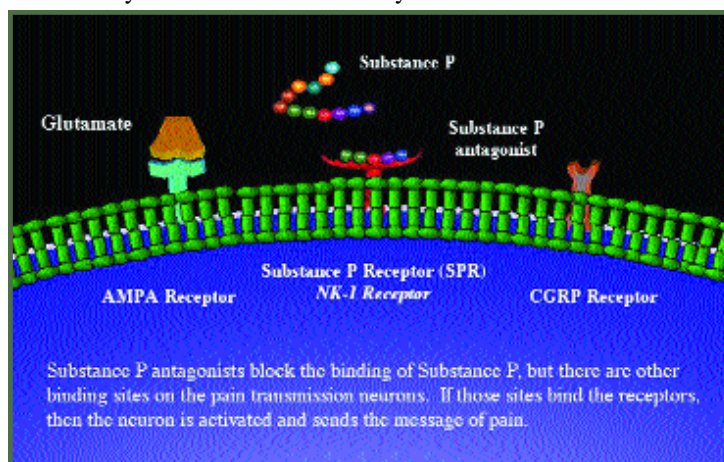
As most of you know, SP-SAP is a potential therapeutic that ATS is developing for use in the elimination of chronic pain. For the past seven years, preclinical studies have been carried out in the rat, safety and dosing studies completed in the dog and the first of two toxicology studies has begun in the rat. The second study is due to start later this year.

SP-SAP is a conjugate of the peptide, Substance P, and the ribosome-inactivating protein, saporin. It has been shown in all the recognized animal models of pain to eliminate the chronic pain signal. The acute (normal) pain signal remains intact. The removal of the chronic pain signal is permanent with no discernible side effects.

SP-SAP works by specifically removing the neurons in the spinal cord that express the Substance P (NK-1) receptor. This represents about 5% of the population of neurons in that area. Administration is through intrathecal injection, similar to the epidural used in childbirth.

Years ago, when the role of substance P in the transmission of the signal for pain became clear, it was immediately proposed by pharmaceutical scientists to construct analogs of substance P that would block the ability of it to bind to its receptor (see illustration). It was hypothesized that these antagonists would bring about pain relief. However, these analogs have always been disappointing. The reason for this may be that the pain pathway is very important and there are several redundancies; there are several other neurotransmitters, both peptides such as somatostatin or CGRP and smaller molecules such as glutamate, that are involved in transmission of the signal. Hence, blocking one of them is not sufficient; the others step in and take their place.

ATS is actively meeting with pharmaceutical companies to select the right partner to bring SP-SAP to market. There is a great unmet need among people throughout the world who are suffering from chronic pain. SP-SAP could bring these people a better quality of life. With the right partner, SP-SAP could be in clinical trial in a year.



## Targeting Teaser Winners

Congratulations to the puzzle solvers from our last newsletter. Each winner receives \$100 credit towards research product purchases from Advanced Targeting Systems.

### The solution to the puzzle was:

Jumbles: PHEROMONE  
ODORANT  
CIRCUIT  
STOCKHOLM  
BIOPHYSICS

Answer: LINDABUCK

### WINNERS:

Bryan Hudson, Washington State University \*  
Kim Van Vliet, University of Florida \* Michael  
Lebowitz, Panacea Pharmaceuticals Inc. \* Mark  
Weiss, Kansas State University \* Robert Speth,  
University of Mississippi \* Seto  
Chice, SUNY HSC  
at Brooklyn \*  
Andreas Lehner,  
University of Kentucky



**Linda Buck** was the recipient of the 2004 Nobel prize in physiology or medicine. Dr. Buck is a member of the Fred Hutchinson Cancer Research Center's Basic Sciences Division, investigator for the Howard Hughes Medical Institute, and affiliate professor of physiology and biophysics at the University of Washington School of Medicine. She received the award in Stockholm for her work on odorant receptors and the structure of the olfactory system.

Dr. Buck is honored for discovering the molecular basis of smell: a multigene family that encodes 1,000 different olfactory receptors in the nose. She shared the prize with Dr. Richard Axel of Columbia University. Their work is the first to define the genes and proteins that control the complex odorant response. They were able to carry out this remarkable work by developing a genetic method to visualize a neural circuit.

Buck also discovered and characterized families of receptors for pheromones and tastes, providing insights into the mechanisms underlying pheromone effects and taste perception.