## Saporin Immunotoxins for Treating Human Hematological Malignancies

(continued from page 2)

level up. The trial continues in this way until the MTD is reached. In our ongoing studies with OKT10-SAP in adult myeloma patients a dose level of 40  $\mu$ g/kg/day x 5 days has been reached so far without any serious drug-related side effects. Encouragingly, we have not encountered vascular leak syndrome in any patient. Approximately half of the patients have developed human anti-mouse antibodies (HAMA) and a similar number human anti-saporin antibodies (HASA). Pharmacokinetic analysis, though only partially completed and not yet formally analyzed, has revealed some major differences in peak levels and decay rates between different patients. This probably reflects differences in tumor burden between individual patientsit is predicted that patients with higher tumor burdens will achieve lower peak serum levels and a shorter drug half life due to rapid removal of drug from the circulation by the larger antigenic "sink" that a larger



Figure 4. Children with relapsed acute lymphoblastic leukaemia are now being treated at eleven different children's cancer centres around the United Kingdom.

tumor burden provides. The BU12-Saporin study in relapsed pediatric ALL is at a less advanced stage and has so far recruited six patients. Once the MTD has been established for both drugs then we can move on to Phase II studies whose primary objective will be to determine the response rate. Then the really exciting work begins!

## REFERENCES

- Vitetta ES, Thorpe PE, Uhr JW (1993) Immunotoxins: Magic Bullets or Misguided Missiles? *Immunol Today* 14:252-259.
- Vitetta ES, Stone M, Amlot P et al. (1991) Phase I immunotoxin trial in patients with B-cell lymphoma. *Cancer Res* 51:4052-4058.
- Falini B, Bolognesi A, Flenghi L et al. (1992) Response of refractory Hodgkin's disease to monoclonal anti-CD30 immunotoxin. Lancet 339:1195-1196.
- Gould BJ, Borowitz MJ, Groves ES et al. (1989) Phase I study of an anti-breast cancer immunotoxin by continuous infusion: Report of a targeted toxic effect not predicted by animal studies. J Natl Cancer Inst 81(10):775-781.
- Flavell DJ, Noss A, Pulford KA, Ling N, Flavell SU (1997) Systemic therapy with 3BIT, a triple combination cocktail of anti-CD19, -CD22, and -CD38-saporin immunotoxins, is curative of human B-cell lymphoma in severe combined immunodeficient mice. *Cancer Res* 57(21):4824-4829.
- Flavell DJ, Boehm DA, Noss A, Warnes SL, Flavell SU (2001) Therapy of human T-cell acute lymphoblastic leukaemia with a combination of anti-CD7 and anti-CD38-SAPORIN immunotoxins is significantly better than therapy with each individual immunotoxin. *Br J Cancer* 84(4):571-578.
- Messmann RA, Vitetta ES, Headlee D et al. (2000) A phase I study of combination therapy with immunotoxins IgG-HD37-deglycosylated ricin A chain (dgA) and IgG-RFB4-dgA(Combotox) in patients with refractory CD19(+), CD22(+) B cell lymphoma. *Clin Cancer Res* 6(4):1302-1313.

## Targeting Ticklers Thoughts to Ponder

Why are a wise man and a wise guy opposites?

If horrific means to make horrible, does terrific mean to make terrible?

Why isn't 11 pronounced onety-one?

If a pig loses its voice, is it disgruntled?

If love is blind, why is lingerie so popular?

When someone asks you, "A penny for your thoughts," and you put your two cents in, what happens to the other penny?

Why do we say something is out of whack? What is a "whack"?

Why is the man who invests all your money called a broker?

Why do croutons come in airtight packages? It's just stale bread to begin with.

If you mixed vodka with orange juice and milk of magnesia, would you get a Phillips Screwdriver?

"I am" is reportedly the shortest sentence in the English language. Could it be that "I do" is the longest sentence?

If lawyers are disbarred and clergymen defrocked, doesn't it follow that electricians can be delighted, musicians denoted, cowboys deranged, models deposed, tree surgeons debarked and dry cleaners depressed?

## 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:

THROUGHP	UT LYMPHOMA
ELECTRON	GENETICIST
DIALYSIS	

Answer:

Jumbles:

Why the scientist was excited to hear his agriculture grant was funded — IT WOULD HELP HIM GET "AHEAD"

WINNERS:

Dr. Chris Flores, Univ Texas Health Science Center, Endontics \* Lauren Phillips, Univ Texas Health Science Center, Pharmacology \* Dr. Venky Ramakrishna, Argonex Inc \* Mark Aitkenhead, UC Irvine, Bio Sci \* Dan Binder, Univ Virginia, Psychobiology \* Joseph Menonna, E Orange VAMedical Center, Neurology Service \* Robert Speth, Washington State Univ, VCAPP