July 2002
Volume 3, Issue 3

Targeting Trends

Reporting the latest news in Molecular Surgery

Saporin Immunotoxins for Treating Human Hematological Malignancies

Contributed by David J Flavell, PhD, The Simon Flavell Leukaemia Research Unit, Division of Cancer Sciences, University of Southampton Medical School, United Kingdom.

I have asked Dr. Flavell to contribute an article on the clinical use of his saporin immunotoxins. Dr. Flavell's research unit is named after his son, who died from leukemia. At that point, he and his wife, Bee, dedicated their lives to finding a cure for childhood cancers. You are encouraged to contribute to Dr. Flavell's efforts that are more fully described at the following website:

www.leukaemiabusters.org.uk.

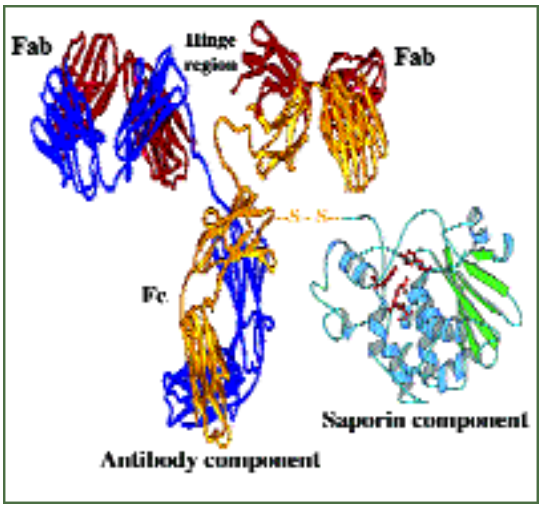
Douglas A. Lappi,
President/Chief Scientific Officer

Immunotoxins have a clinical utility in any human condition where the elimination of an unwanted cell population is desired. The most obvious candidate disease is cancer and consequently the vast majority of early phase clinical studies with immunotoxins have centered on the treatment of human malignancies with the goal of eliminating cancer cells from the patient's body. Most of these clinical trials have been conducted using ricin A chain or blocked ricin[1] as the toxin component. Whilst there have been anti-tumor responses with ricin-based immunotoxins, particularly in hematological malignancies,[2] their toxicity profile has limited their clinical usefulness and interest in their utility has consequently dropped away. In contrast, there have been very few clinical studies with saporin-based immunotoxins (Fig 1). The earliest study was conducted by Falini and his associates[3] in Italy and Germany utilizing a CD30 antibody coupled to saporin for the treatment of four patients with advanced Hodgkin's disease. Two patients showed dramatic responses to treatment and no serious side effects were observed. In particular, vascular leak syndrome, a potentially fatal toxicity that had been associated with ricin-based immunotoxins, was not observed.

These initial results encouraged us to undertake preclinical investigations with immunotoxins directed against the B-cell restricted CD19 antigen for B-lymphoid tumors and against the CD38 molecule for multiple myeloma. The development of such therapeutic molecules required robust preclinical investigations to determine their toxicity profiles in animals, the normal

(continued on page 2)

Figure 1. Idealized molecular ribbon diagram of the appearance of an immunotoxin with saporin coupled covalently via a disulfide bond to a mouse monoclonal antibody.



Inside this issue:

Newsletter Highlights

- Featured Antibodies *(page 3 and page 4)*
- Neuropeptide Toxins *(page 5)*
- Anti-Tac and Anti-Tac-SAP *(page 7)*

Denise Higgins, Editor

ADVANCED TARGETING SYSTEMS