Human Antibodies 12 (2003) 25–26
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Session 9: Applied technologies – I

Friday 10 October 2003. Moderators: Larry Green and Mark Glassy

[08.30–09.00]
[Keynote Lecture]
Therapeutic fully human antibodies for cancer and infectious diseases
Shiro Kataoka
Kirin Brewery Company Ltd, Tokyo, Japan

Abstract not received.

[09.00–09.30]
Formatting antibody fragments to mediate specific therapeutic function
Dee Athwal
CELLTECH, Slough, Berkshire, UK

The intrinsic properties of antibodies have resulted in them becoming widely exploited as tools in both basic research and the treatment of human disease. This has been made possible through our increased understanding of the relationship between antibody structure and antibody function. With this understanding, we are now beginning to see an increasing interest in the development of alternatives to whole IgG as the human therapeutics. In some instances a move away from the IgG scaffold itself.

For the treatment of human disease, it is desirable that drug discovery and development process offers a speedy route to the clinic and market. The selected lymphocyte antibody method (SLAM) enables the selection of very high affinity antibodies by rapid screening of the entire immune repertoire of any mammal. As such, SLAM offers significant advantages over conventional hybridoma technology for the rapid selection of high affinity functional antibodies in greatly reduced timeframes.

By reference to antigens including CD134 and IL-1β, this talk will reveal how SLAM, when combined with the ability to examine the *in vivo* function of antibody derivatives that vary valency and Fc function, can increase the likelihood of therapeutic success.

[09.30–10.00]
Exploiting the immune diversity of XenoMouse® mice for discovery of antibody product leads
Larry L. Green
Abgenix, Inc. 6701 Kaiser Drive, Fremont, CA 94555, USA

The discovery process for antibody-based therapeutics starts with definition of design goals for the product, which sets the course for all the subsequent steps of the program. The process then proceeds to generation and recovery of a large panel of target-binding antibodies, which may be winnowed early based on specificity or affinity requirements. Next, the entire pool or a subset thereof can be interrogated in high throughput functional assays to identify those mAbs that mediate desired activities. This panel of functional mAbs can be further parsed based on potency or fine structure criteria including antibody sequence or target epitope. From this smaller pool, lead candidates can be tested in lower throughput in vivo assays for function and toxicity, leading to the choice of the candidate and back-ups for human clinical trials.

Abgenix has built an efficient process for discovery of therapeutic product leads based on the above paradigm. The XenoMouse technology lies at the heart of antibody discovery at Abgenix. XenoMouse mice are strains of mice in which the endogenous murine immunoglobulin genes have been inactivated and functionally replaced by human immunoglobulin transgenes that encompass the majority of the human repertoire. XenoMouse mice make fully human IgGκ and IgGλ antibodies of affinity, potency and composition suitable for human therapeutics. Utilizing an optimized hybridoma process, dozens to over a thousand high affinity antigen-specific monoclonal antibodies can be recovered directly from hyperimmunized XenoMouse animals. The immortalized and genetically stable hybridomas provide scalability for producing material sufficient for a rapid discovery of product leads. Choosing from a menu of technologies, the

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mAbs are tested for cross-reactivity, functionality, potency, affinity, sequence and epitope characteristics in a plan of work tailored to the unique needs of each product discovery effort.

[10.00–10.20]
Title to be confirmed
Larry Zeitlin
Epicyte Pharmaceuticals Inc, USA

Abstract not received.