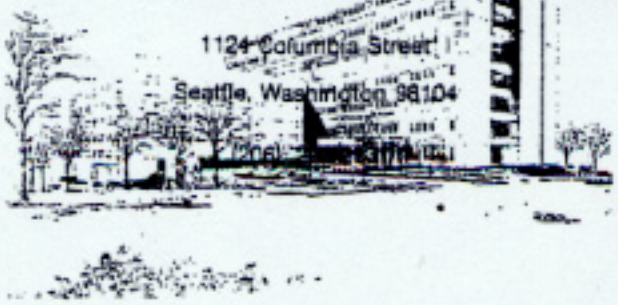
FRED HUTCHINSON CANCER RESEARCH CENTER



FRED HUTCHINSON CANCER RESEARCH CENTER

HUMAN SUBJECTS REVIEW COMMITTEE

MINUTES

MEETING: A special meeting was held February 12, 1981 in the West Conference Room of the Fred Hutchinson Cancer Research Center.

MEMBERS PRESENT:
Dr. Donald Tesh, Chairman
Dr. Kristine Doney
Dr. Michael Kennedy
Mrs. Ethel Hopkins
Rev. Richard Johnson
Ms. Diana McCann *
Dr. Lincoln Polissar
Dr. Vernon Riley
Ms. Janet Schwarz, R.N.
Mr. Val Tollefson

*Standing in for Dr. Ensinck.

GUESTS:
Dr. John Hansen
Dr. Paul Morton
Dr. Robert Nowinski
Dr. Beverly Torok-Storb
Dr. E. Donnal Thomas
Mrs. Dorothy Thomas

MEMBERS ABSENT:
Dr. John Ensinck
Dr. Meredith Smith

The meeting was called to order at 4:10 p.m.. Purpose of this special meeting was to aquaint Human Subjects Review Committee members with Hybridoma Technology and it's clinical application. Also to be addressed were specific questions relating to Dr. John Hansen's proposed protocol H811-180N, "Prevention of Graft Versus Host Disease (GVHD) by Deleltion in Vitro of Donor "T"-Cell with Mono-Clonal Antibody and Complement."

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Dr. Thomas lead the presentation by demonstrating that the theory behind the use of Monoclonal Antibody serum is nothing new to the treatment of GVHD or to the committee members. Protocols using Antithymocyte Globulin (ATG) date back to 1972. This technique involved the injection of Thymocytes into horse, goat or rabbit antibody to produce a serum. Once purified, the ATG was administered in four milligram doses over a relitively long period of time. One problem with ATG is that it is not pure enough to be specific.

Dr. Nowinski, who along with Dr. Bernstein, has been perfecting the technique of getting pure specific antibody, followed Dr. Thomas. He built on Dr. Thomas' point that the major obstacle has been the difficulty of getting pure antibody. Whether harvested from the blood of patients undergoing diagnosis or from animals stimulated to produce it, (as with ATG) the antibody in question is invariably mixed with many, many other antibodies in the blood. The use of Hybridomas or Monoclonal Antibody eliminates this problem. Now it is possible to specify the desired antibody which reacts to a specific cell and to obtain it in an abundant and purified form.

Dr. Hansen's protocol targets natural Lymphocites found in the donors bone marrow. These cells, when introduced into a recipiant with no immune capability, attack the host or receiving patient as if it were a foreign body. Dr. Hansen proposes to use Monoclonal Antibody to destroy the donors Lymphocites or T cells thus allowing only purified marrow to be given to the patient.

QUESTION: Dr. Nowinski's work has been demonstated successfully in the mouse, but how does this relate to humans? Shouldn't the technique be proven on higher animals first? Dr. Storb stated that work was being done on dogs. However, Dr. Nowinski pointed out that no matter what animal model is used the result will be the same. At the same time, you cannot produce an antibody directed to a human cell and test it on a dog or a monkey or a mouse. The Monoclonal Antibody is only specific for that species from which it was derived. Therefore, no matter how much work is done in lower animals it still must be done anew in man.

QUESTION: Should not the F.D.A. be involved? Dr. Thomas stated that he has tried in the past to get the F.D.A. involved in ATG studies, but they declined. In fact they will depend on the leaders in the field for information. In this field of Monoclonal Antibody we and several others are the leaders. However, Ortho does have an IND for their Monoclonal Antibody OKT-3 which they intend to market.

QUESTION: Should this committee be concerned about the problems with proper review at U.C.L.A.? Dr. Thomas replied that there really is no relationship between F.H.C.R.C.'s Review Committee and U.C.L.A.'s committee. There the investigators have accused the committee of dictating the practice of medicine and the Review Committee is accusing the investigators of not submitting protocols. Our relationship with the Medical Oncology group has always been good. They have always submitted protocols for review, even under emergency conditions or on rare occasions, and have always done their best to comply with recommendations.

QUESTION: Are there any other patient related studies going on? Dr. Peter Wright, although not present, had reported to John Mills that under the study approved in June (H804-139N) he has enrolled six melanoma patients. Several of these patients have received up to five doses without evidence of toxicity due to mouse antigens.

Dr. Hansen stated that both Stanford Research Institute and Ortho had antibodies like his 9.6 and 10.2, and that pre-clinical and clinical trials were underway. Stanford, using their LOU-1, had enrolled four patients using a technique similar to the one he proposes. Although still early, there is no reported adverse effect. Also, Ortho laboratory, using their OKT-3, are treating renal transplant patients at Massachusetts General Hospital.

Dr. Hansen also stated he now plans to modify the H811-180N protocol to include both his Monoclonal Antibody and a commercial antibody.

QUESTION: Has there been any "Peer Review"? Dr: Hansen reported that his work as well as that of Dr. Storb and others had been reviewed on February 9th and 10th, by an N.C.I. site visit team. The work met with general approval and excitement by the site visit team members.

QUESTION: Will this procedure destroy the patients chances of a second engraftment should the first fail? Dr Thomas responded by saying that a second conditioning regimen would not be required. The only risk is exposure to a low cell count for an additional 14 days. This has not proved to be a difficult problem in the past.

The meeting closed with committee discussion to be taken up at the February 17, 1981 meeting.

Respectfully submitted,

Donald W. Tesh

DONALD W. TESH, M.D.
Chairman, Human Subjects Reveiw
Committee

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