DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

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National Cancer Institute
Bethesda, Maryland 20892

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Dr. Abdelkrim Alileche
Albert Einstein College of Medicine
Immunology Microbiology Department
Room G404
1300 Morris Park Avenue
Bronx, New York 10469

RE: Dr. Abdelkrim Alileche

To Whom It May Concern:

I offer my enthusiastic recommendation in support of Abdelkrim Alileche's application for a staff position. Dr. Alileche joined the Metabolism Branch and worked directly with me from March 1994 until 1998. He worked on three projects: (1) the development of a new model for the induction of IL-2 receptor alpha chain by IL-2 and IL-15, (2) the production of a monoclonal antibody against the IL-2 receptor gamma chain, and (3) the search for an alternative to the IL-2 receptor gamma chain.

One of our primary interests relates to the regulation of the immune responses and disorders of these regulatory mechanisms that underlie immunodeficiency and lymphoid malignancy. These research studies are directed toward defining the nature of immunoregulatory disorders and the molecular biological abnormalities that underlie immunodeficiency and neoplastic disease. We translate our basic research on disease pathogenesis into the preclinical development of new therapeutic agents. The new drugs that are the most successful in preclinical therapeutic models are then used in our clinical trials at the National Institutes of Health. Clinical research is directed toward developing rational approaches for the treatment of cancer, primary immunodeficiency disease, and AIDS.

In March 1994, Dr. Alileche joined my group in the Metabolism Branch, National Cancer Institute for a 4-year period. He focused on the production of a monoclonal antibody against the human γc. Using molecular biological techniques he cloned many fragments of the γc chain and linked them to the GST protein. These efforts led to the production of the monoclonal antibody 47C7/C7, an antibody that recognizes a juxtamembranous domain of the γc. In that regard, 47C7/C7 is similar to 7G7/B6 and HIEI (Mabs against a similar region of the IL-2Rα chain). In collaboration with Dr. Sandor Damjanovich, Dr. Alileche, using the very sophisticated fluorescence energy transfer (FRET) technology, demonstrated that 47C7/C7 recognizes the γc. Using comparative studies with 47C7/C7 and TUGH4 (Mab to the γc produced by Sugamura's lab), he found that Adult T-cell leukemia cells (HuT-102, MT-2), which express the γc are stained by 47C7/C7 but not by TUGH4. Furthermore, there was a non-random association of γc with IL-2Rα before the addition of cytokine. In addition, 47C7/C7 was

able to recognize a soluble recombinant γc when assessed with an ELISA assay. Therefore, the 47C7/C7 antibody is a valuable tool to study the IL-2R as well as those other receptors using the γc (e.g., IL-4R, IL-7R, IL-9R, IL-15R and IL-21R).

Subsequently, Dr. Alileche developed a new model for the induction of the IL-2Rα chain. Since the α chain is the private receptor for IL-2, its expression is very important for the formation of the high-affinity receptor for IL-2. IL-2 and IL-15 can bind to the βγc complex of the IL-2/IL-15 receptors. Dr. Alileche demonstrated by using purified large granular lymphocytes (LGL) cells that both IL-2 and IL-15 can induce the mRNA for the α chain. Furthermore, for both cytokines this mRNA is translated into IL-2Rα protein as demonstrated by ELISA assays using cell lysates. However, only IL-15 addition induced cell surface expression of the α chains as assessed by FACS analysis. Dr. Alileche described the same phenomenology with two other cell lines YT-1 and TF-1B. This model is interesting because the induction of the key IL-2Rα chain does not require the context of antigen presentation.

Dr. Alileche is an exceedingly motivated scientist who works exceedingly hard on the very difficult research efforts that he chooses to pursue. I am sure that he will continue to make major contributions to the field of immunology and give him my unqualified support for a position with your institution.

Sincerely yours,

Thomas A. Waldmann, M.D.
Chief, Metabolism Branch, NCI, CCR
10 Center Drive, MSC 1374
Building 10, Room 4N115
National Institutes of Health
Bethesda, MD. 20892-1374
Phone: (301) 496-6656; Fax: (301) 496-9956
EM: tawald@helix.nih.gov