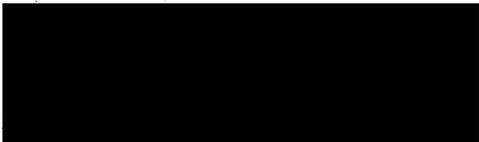




U.S. Citizenship
and Immigration
Services



FILE: WAC 03 085 51431 Office: CALIFORNIA SERVICE CENTER Date:

IN RE: Petitioner:
Beneficiary



DEC 27 2004

PETITION: Immigrant Petition for Alien Worker as a Member of the Professions Holding an Advanced Degree or an Alien of Exceptional Ability Pursuant to Section 203(b)(2) of the Immigration and Nationality Act, 8 U.S.C. § 1153(b)(2)

ON BEHALF OF PETITIONER:



PUBLIC COPY

INSTRUCTIONS:

This is the decision of the Administrative Appeals Office in your case. All documents have been returned to the office that originally decided your case. Any further inquiry must be made to that office.

Robert P. Wiemann, Director
Administrative Appeals Office

identifying data deleted to
prevent clearly unwarranted
invasion of personal privacy

B-5

DISCUSSION: The employment-based immigrant visa petition was denied by the Director, California Service Center, and is now before the Administrative Appeals Office on appeal. The appeal will be sustained, and the petition will be approved.

The petitioner seeks classification pursuant to section 203(b)(2) of the Immigration and Nationality Act (the Act), 8 U.S.C. § 1153(b)(2), as a member of the professions holding an advanced degree. At the time of filing of the petition, the petitioner was working as a researcher in the Department of Cellular and Molecular Medicine at the University of California, San Diego. The petitioner asserts that an exemption from the requirement of a job offer, and thus of a labor certification, is in the national interest of the United States. The director found that the petitioner qualifies for classification as a member of the professions holding an advanced degree, but that the petitioner had not established that an exemption from the requirement of a job offer would be in the national interest of the United States.

Section 203(b) of the Act states in pertinent part that:

(2) Aliens Who Are Members of the Professions Holding Advanced Degrees or Aliens of Exceptional Ability. --

(A) In General. -- Visas shall be made available . . . to qualified immigrants who are members of the professions holding advanced degrees or their equivalent or who because of their exceptional ability in the sciences, arts, or business, will substantially benefit prospectively the national economy, cultural or educational interests, or welfare of the United States, and whose services in the sciences, arts, professions, or business are sought by an employer in the United States.

(B) Waiver of job offer.

(i) Subject to clause (ii), the Attorney General may, when the Attorney General deems it to be in the national interest, waive the requirements of subparagraph (A) that an alien's services in the sciences, arts, professions, or business be sought by an employer in the United States.

The director found that the petitioner qualifies as a member of the professions holding an advanced degree. The sole issue in contention is whether the petitioner has established that a waiver of the job offer requirement, and thus a labor certification, is in the national interest.

Neither the statute nor regulations define the term "national interest." Additionally, Congress did not provide a specific definition of "in the national interest." The Committee on the Judiciary merely noted in its report to the Senate that the committee had "focused on national interest by increasing the number and proportion of visas for immigrants who would benefit the United States economically and otherwise. . . ." S. Rep. No. 55, 101st Cong., 1st Sess., 11 (1989).

Supplementary information to regulations implementing the Immigration Act of 1990 (IMMACT), published at 56 Fed. Reg. 60897, 60900 (November 29, 1991), states:

The Service believes it appropriate to leave the application of this test as flexible as possible, although clearly an alien seeking to meet the [national interest] standard must make a showing significantly above

that necessary to prove the "prospective national benefit" [required of aliens seeking to qualify as "exceptional.""] The burden will rest with the alien to establish that exemption from, or waiver of, the job offer will be in the national interest. Each case is to be judged on its own merits.

Matter of New York State Dept. of Transportation, 22 I&N Dec. 215 (Comm. 1998), has set forth several factors which must be considered when evaluating a request for a national interest waiver. First, it must be shown that the alien seeks employment in an area of substantial intrinsic merit. Next, it must be shown that the proposed benefit will be national in scope. Finally, the petitioner seeking the waiver must establish that the alien will serve the national interest to a substantially greater degree than would an available U.S. worker having the same minimum qualifications.

It must be noted that, while the national interest waiver hinges on *prospective* national benefit, it clearly must be established that the alien's past record justifies projections of future benefit to the national interest. The petitioner's subjective assurance that the alien will, in the future, serve the national interest cannot suffice to establish prospective national benefit. The inclusion of the term "prospective" is used here to require future contributions by the alien, rather than to facilitate the entry of an alien with no demonstrable prior achievements, and whose benefit to the national interest would thus be entirely speculative.

Eligibility for the waiver must rest with the alien's own qualifications rather than with the position sought. In other words, we generally do not accept the argument that a given project is so important that any alien qualified to work on this project must also qualify for a national interest waiver. At issue is whether this petitioner's contributions in the field are of such unusual significance that he merits the special benefit of a national interest waiver, over and above the visa classification sought. By seeking an extra benefit, the petitioner assumes an extra burden of proof. A petitioner must demonstrate a past history of achievement with some degree of influence on the field as a whole. *Id.* at note 6.

Along with documentation pertaining to his field of research, the petitioner submitted several letters of support.

Dr. Jeffrey Esko, Professor, Department of Cellular and Molecular Medicine, University of California, San Diego, states:

Heparin has been used clinically as an anticoagulant and antithrombotic agent for over 60 years. Heparin also has potent anti-inflammatory properties, but the mechanism of its action was unknown until [the petitioner's] recent work. After extensive study, he found that (i) heparin's anti-inflammatory effects are mainly mediated by blocking a class of cell adhesion receptors called selectins; (ii) specific sulfate groups on heparin play a critical role in selectin inhibition; and (iii) heparin can be converted to a non-anticoagulant form that retains anti-inflammatory activity. His outstanding work on heparin's anti-inflammatory mechanism was very recently published in the prestigious peer-reviewed *Journal of Clinical Investigation*. He developed a nonanticoagulant heparin analog missing certain sulfate groups, which may prove useful as a therapeutic agent to block inflammation. Conceivably, non-anticoagulant heparin could be used to prevent tumor metastasis as well, since the spread of cancer also seems to depend on selectin receptors.

The record contains evidence showing that the article appearing in the *Journal of Clinical Investigation* (which the petitioner first-authored) has been cited at least 20 times.

Dr. [REDACTED] Vice President of Research, and Professor and Head, Division of Vascular Biology, La Jolla Institute for Molecular Medicine, states:

[The petitioner] developed a novel assay for the diagnosis of heparin-induced thrombocytopenia in the laboratory. This piece of work enabling the rapid diagnosis of heparin-induced thrombocytopenia further enhances the overall clinical management of heparin-treated patients.

* * *

[The petitioner's] ongoing research in the laboratory of Dr. [REDACTED] focuses on the role of heparin/heparan sulfate in inflammation. During the last two years, he discovered that the anti-inflammatory effect of heparin is mainly achieved by blockade of L- and P- selectin-mediated cell adhesion, and that 6-O-sulfation of glucosamine residues in heparin are critical for heparin's anti-inflammatory activity. This work may lead to the development of non-anticoagulant forms of heparin as novel anti-inflammatory drugs.

Very recently [the petitioner's] work demonstrated the pivotal role of endothelial heparan sulfate in inflammatory responses *in vivo*. As inflammation is common to almost every disease, this work lays the basic foundation for the management of inflammatory diseases in general. [The petitioner's] work is not only at the cutting edge in the area of glycobiology, but also has the potential for uncovering heparin/heparan sulfate-based drugs for treating inflammatory diseases.

Dr. [REDACTED] Professor and Director of Glycobiology at the Burnham Institute, La Jolla, California, states:

After joining Dr. [REDACTED] laboratory at the University of California, San Diego, [the petitioner] has been working on the anti-inflammatory mechanism of heparin, one of the most heavily used drugs in the world, and on the role of endothelial heparan sulfate in inflammation. His recent work has unraveled the anti-inflammatory effects of heparin. His work showed that this activity is related to heparin's interaction with a class of cell adhesion receptors, known as the selectins. In addition, he showed that one can make chemical derivatives of heparin that lack anti-coagulant activity yet still retain anti-inflammatory activity, which could lead to a new heparin-based anti-inflammation drug. As it is well known that selectins are also critical for tumor metastasis, the new form of heparin could also be used to prevent tumor metastasis.

* * *

Very recently, [the petitioner] made significant progress in understanding the role of endothelial heparan sulfate in inflammation. By using gene knockout technique, he has provided *in vivo* evidence that endothelial heparan sulfate plays pivotal roles in inflammatory response.

Dr. [REDACTED] Professor of Medicine, University of Heidelberg, states:

[The petitioner] developed a novel fluorescence-linked immunofiltration assay (FLIFA) by using normal pooled serum as the source of all the heparin-binding proteins and heparin-Fitc as the signal carrier. This assay mimics the pathological reaction of HIT [heparin-induced thrombocytopenia] *in vivo* and provides accurate information for clinical diagnosis of HIT. In addition, another great advantage of the assay is the speed. The FLIFA assay gives results within 2-3 hours, while the other methods needs 5 hours to two days to finish the assay Based on [the petitioner's] work, my laboratory has been established as one Center for laboratory diagnosis of HIT in Germany. As well the scientific value in this field is obvious. All these work was published [sic] in peer-reviewed, prestigious journals, such as *Journal of Immunological Methods*, *European Journal of Clinical Investigation*, *Thrombosis and Haemostasis*, *Allergy*, et al.

At the same time, he initiated and worked on the study on antigenicity of recombinant hirudin (r-hirudin) in HIT patients The specific antibody to r-hirudin was generated very rare. However, there was no study done with HIT patients at this point. [The petitioner's] studies showed that more than 60% of HIT patients generate specific anti-r-hirudin antibodies. This means that r-hirudin has strong antigenicity in HIT patients, and the treatment of HIT patients with r-hirudin needs to be monitored for generation of the specific antibody Thus the treatment of HIT patients with positive anti-hirudin antibody may have to be revised, and optimize r-hirudin therapeutical effect for HIT patients individually. His work was published in *Circulation*, the number 1 journal on cardiovascular system, and other leading journals in Hematology This work was also confirmed internationally by other groups and cited by many papers.

The record contains evidence showing that the article appearing in the *Circulation* has been cited at least 35 times.

When judging the influence and impact that the petitioner's published work has had, the very act of publication is not as reliable a gauge as is the citation history of the published works. Publication alone may serve as evidence of originality, but it is difficult to conclude that a published article is important or influential if there is little evidence that other researchers have relied upon the petitioner's findings. In this case, the petitioner has provided citation indices for several of his published articles. The substantial number of cites to the petitioner's articles demonstrates widespread interest in, and reliance on, his work. These citation indices show that many other researchers in the United States and from around the world have acknowledged the petitioner's influence and found his work to be significant.

The director requested further evidence that the petitioner had met the guidelines set forth in *Matter of New York State Dept. of Transportation*. In response, the petitioner provided additional letters of support.

Dr. Steven Rosen, Professor, Department of Anatomy, University of California, San Francisco, states:

In [the petitioner's] recent publication in *Journal of Clinical Investigation*, he found that the anti-inflammatory effects of heparin are through its blocking of P- and L-selectin mediated leukocyte adherence. This work enabled us to understand the molecular mechanism of heparin's anti-inflammatory effects These findings are leading to the development of 3-O-desulfate, 6-O-sulfated heparins as novel, heparin-based drugs to treat inflammatory disorders. Selectins are critical for tumor

metastasis too. Based on [the petitioner's] finding, these newly formed, non-anticoagulant heparins can be used to prevent tumor metastasis.

* * *

By using tissue-specific knockout technique, [the petitioner] generated mice that had greatly reduced sulfation modification of endothelial heparan sulfate chain. He found these mice have an impaired inflammatory response. This work demonstrates that endothelial heparan sulfate plays an important role in the inflammatory response. This is the first *in vivo* evidence of its kind. It is a major step forward and will have a high impact in our field. Subsequently, [the petitioner] found out that impaired inflammatory response resulted mainly from decreased chemokine binding on luminal surface of endothelium. According to this work, interruption of chemokine binding on endothelial luminal surface should be an effective way to treat inflammatory diseases. This contribution may lead to new approaches, such as using heparan sulfate analogs and specific heparan sulfate biosynthesis inhibitors, to block chemokine binding, and thus to treat inflammatory disorders.

In summary, [the petitioner's] work elucidated the molecular mechanism of heparin's anti-inflammatory effect, structure-function relationship of the activity, and the critical roles of endothelial heparan sulfate in inflammatory reaction. This work provides clear strategies to develop novel anti-inflammatory drugs.

Dr. [REDACTED] Associate Professor, Department of Immunology, The Scripps Research Institute, states:

[The petitioner] came to my attention because of his work on the anti-inflammatory mechanism of heparin and characterization of the sulfation pattern of heparin required for the anti-inflammatory activity. The strategy he used to characterize the structural requirement of heparin's anti-inflammatory effects is a good sample for people to study the interaction of heparin with its ligands. Through this work, [the petitioner] found that the 6-O-sulfation of heparin glucosamine is required to retain its potent anti-inflammatory activity. According to this finding, non-anticoagulant heparin, like 2-O, 3-O-desulfated heparin, and N-desulfated heparin can be developed into novel anti-inflammatory drugs. By using selectin-deficient mice with various inflammation models, [the petitioner] found that heparin's anti-inflammatory effects *in vivo* is achieved mainly by blocking L- and P-selectin mediated leukocyte migration in the inflammatory response Through the same mechanism, these newly formed heparins can be used to prevent tumor metastasis. These achievements were published in the top biomedical journal, *The Journal of Clinical Investigation* and received attention from both clinical doctors and pharmaceutical companies.

* * *

[The petitioner] produced mice with lowly sulfated endothelial heparan sulfate To date, [the petitioner's] data showed that these deficient mice have decreased inflammatory response, which results from the impaired chemokine binding and presentation to rolling leukocytes on the luminal surface of endothelium. This study provides the first *in vivo* evidence that endothelial heparan sulfate is required for inflammatory response. This work improves our basic understanding of inflammation in general, and also opens a research area with great potential for the discovery of new anti-inflammatory drugs. In

addition, his deficient mice, also for the first time, offer the possibility of studying the role of endothelial heparan sulfate in other critical pathological processes, such as tumor growth, tumor metastasis, angiogenesis, wound healing, hemostasis and HIV infection *et al.* His contributions are therefore of major significance and have extensive influence in these related fields.

Dr. Mortimer Poncz, Professor of Pediatrics, University of Pennsylvania School of Medicine, states:

I do not know [the petitioner] personally, but I know his work quite well through his publications.

* * *

[The petitioner] recently found that in the *in vivo* situation, the anti-inflammatory effects of heparin were mainly due to inhibiting the binding of P- and L-selectins to their natural ligands, which blocked selectin-mediated leukocyte migration in the inflammatory response. It has been known for a long time that 3-O-sulfation modification of glucosamine residue is critical for heparin's anticoagulant activity. The potential anticoagulant activity, the bleeding side-effect, limits heparin's use as anti-inflammatory drug. [The petitioner] found that the 6-O-sulfation modification of glucosamine residue is critically required for its strong anti-inflammatory effect. Based on this work, new heparin lacking 3-O-sulfation with 6-O-sulfation modification can be developed as a novel non-anticoagulant heparin-based anti-inflammatory drug. These new drugs can be used to treat inflammatory diseases, such as arthritis and inflammatory bowel disease. This kind of drug can be used to block P- and L-selectin mediated tumor cell metastasis, the most critical stage of tumor progression.

Dr. [REDACTED] Professor of Biochemistry, University of California, [REDACTED] cites the petitioner's publications and states that he "has conducted outstanding work on the development of a non-anticoagulant heparin for use as a drug in treating chronic inflammation and cancer metastasis."

Dr. [REDACTED] Chief, Molecular Biology of Bones and Teeth Unit, Craniofacial and Skeletal Diseases Branch, National Institutes of Health, states:

I have not met [the petitioner] personally, and I do not directly collaborate with him [The petitioner] studies the anti-inflammatory mechanism of heparin and the structural basis for its roles in the inflammatory response. This is an excellent target to focus on in the fight against inflammatory disorders. To date, [the petitioner] has made significant discoveries in this field. Specifically he found that the anti-inflammatory effects of heparin *in vivo* is achieved by blocking of P- and L-selectin mediated leukocyte migration, and that this activity is critically dependent on the 6-O-sulfation modification of glucosamine residues. This work provides a critical foundation to develop new generation, non-anticoagulant heparins as novel inflammatory drugs.

* * *

Making genetically engineered mice is a powerful tool to study the physiological and pathological roles of some critical molecules *in vivo*. [The petitioner] generated mice lacking endothelial NDST1. NDST1 is the most critical sulfation modification enzyme in heparan sulfate biosynthesis pathway. [The petitioner] observed that the NDST1 deficient mice have an impaired inflammatory response. This is

the first demonstration in live animals that endothelial heparan sulfate plays an important role in inflammation. [The petitioner] also discovered the molecular basis for this. He showed that the NDST1 deficient endothelium has decreased chemokine binding to the luminal surface compared [to] normal endothelium. In the NDST1 deficient mice, the luminal surface bound less chemokine so that there were less leukocytes that could be activated during inflammation. This work points to a new strategy to develop anti-inflammatory drugs where one would use heparin analogs or heparan sulfate biosynthesis inhibitor to block the endothelial heparan sulfate mediated chemokine binding and presentation in inflammation.

The director denied the petition, stating that the petitioner failed to establish that a waiver of the requirement of an approved labor certification would be in the national interest of the United States. The director acknowledged the intrinsic merit and national scope of the petitioner's work, but found that the petitioner's own contribution does not warrant a waiver of the job offer requirement that, by law, attaches to the classification that the petitioner chose to seek.

On appeal, counsel states:

The above testimonial letters from established experts and colleagues, the attraction of co-operations from other independent investigators, high citation frequency of the petitioner's work and invitation of the petitioner as grant reviewer by federal research agency [sic] identified appellant's past and present record of success . . . and how such success laid foundation for future contribution to U.S. national interest.

In this matter, we find that the evidence presented is adequate to meet the three-prong test established by *Matter of New York State Dept. of Transportation*. The large number of cites to the petitioner's published work, along with the statements of witnesses from outside of the petitioner's immediate circle of colleagues, shows that the petitioner's work has advanced his field to a substantially greater degree than that of other similarly qualified researchers. Upon careful consideration of the documentation presented, we find that the petitioner has shown that researchers from throughout his field view his findings as significant breakthroughs in biomedical research.

It does not appear to have been the intent of Congress to grant national interest waivers on the basis of the overall importance of a given field of research, rather than on the merits of the individual alien. That being said, the above testimony, and further evidence in the record, establishes that the greater scientific community recognizes the significance of this petitioner's research rather than simply the general area of research. The benefit of retaining this alien's services outweighs the national interest that is inherent in the labor certification process. Therefore, on the basis of the evidence submitted, the petitioner has established that a waiver of the requirement of an approved labor certification will be in the national interest of the United States.

The burden of proof in these proceedings rests solely with the petitioner. Section 291 of the Act, 8 U.S.C. § 1361. The petitioner has sustained that burden. Accordingly, the decision of the director denying the petition will be withdrawn and the petition will be approved.

ORDER: The appeal is sustained and the petition is approved.