REPORT ON IMMUNOLOGY AND THE NEUROSCIENCES

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Introduction

This report consists of two, complementary parts. The first, published in 1998, includes evaluations of Israeli immunology and neurosciences, based on bibliometrical data and on written evaluations solicited from 2-5 respected world authorities in each field.

The second, published in 1999, comprises the reports of two expert committees convened by the Division of Sciences of the Israel Academy to further investigate the status of these fields. The committees, composed of world authorities in the neurosciences and immunology, respectively, received written material on research in Israeli universities and met with individual scientists during their several-day stay. They then met at the Academy for 1-2 days for discussions and the preparation of their reports.

Part I.
Bibliometric and Initial External Expert Review (1998)

ISRAEL SCIENCE EVALUATION 1996-97: IMMUNOLOGY AND THE NEUROSCIENCES

On Evaluation and Measurement. Recognizing the tremendous potential contributions of science and technology to national development, many countries have placed the evaluation of scientific research high on their agenda. Although it is relatively easy to quantitate such research *inputs* as the number of dollars or scientist-hours invested, it is considerably more difficult to properly quantitate research *outputs*, the national scientific, economic, social and political "return" on such investments. Even restricting oneself to such strictly scientific measures as "impact" and "excellence," meaningful, objective, quantitative analyses are difficult, at the present state-of-the-art, to obtain.

Not only is there considerable controversy over the meaning and usefulness of the various indicators employed, but the evaluation parameters of most significance can vary from country to country. For example, nations aspiring to be world "quantity leaders" will assess their scientific wealth in terms of measures reflecting various aspects of total output. Other countries, particularly small countries such as Israel, while they cannot be quantity leaders, can and must be "quality leaders." For them, it is crucial to evaluate and maintain the quality of their research.

The quantitative indicators currently in use are mostly bibliometrical and are mostly based on data provided, for a fee, by the U.S.-based Institute for Scientific Information (ISI). Their database covers all scientific research papers published in more than 4,000 journals from 79 countries since 1981. The use of such indicators is based on two basic assumptions: (a) the number of scientific publications, variously normalized, is indicative of scientific *activity*; (b) the number of citations per paper, in indicative of the impact of scientific work and thus often

attests to its quality. Both assumptions have their supporters and detractors (for example, published conclusions later proved incorrect will also generate considerable citations and activity).

The usual citation measures are the citation index (CI), the number of times a particular scientific paper was cited by other published papers during a given period, and the *citation impact*, the total CI for a set of papers (e.g., total national output in a given field) divided by the number of publications published in that period. One can calculate the citation impact for different countries, disciplines, etc. and compare them to each other or to an international or cross-field average. The relevant field is usually gleaned from the journal title, except for some broad-interest journals such as *Nature* or *Science*, for which the categorization of each paper must be done "manually." ISI data routinely lists only the first-named author, and makes no distinction between "high prestige" and "low prestige" journals (an important quality criterion among scientists), although special requests can sometimes be honored. While not ideal, and certainly not absolute, these indicators may provide useful information on the relative ranking of countries in various disciplines, and raise unexpected anomalies, trends and concerns for further exploration.

Science Evaluation at the Israel Academy. In 1993 the Council of the Israel Academy of Sciences and Humanities appointed a Committee for Science Policy, which was charged with monitoring and reporting on the development of the Israeli science. It concluded that the Academy should publish periodical reports on the status of Israeli science in a global perspective. Such a report should include quantitative indicators as well as more detailed expert assessments of particular disciplines.

In view of this recommendation, and some preliminary bibliometric presentations, the Academy's Division of Sciences, decided to undertake a more in-depth evaluation of two fields, immunology and the neurosciences, based on both (a) several quantitative indicators and (b) expert field evaluations solicited by letter from respected world-class scientists in the two disciplines studied.

General Background. Israel ranks very high in its share of the world's total number of scientific papers and citations (all fields), normalized to reflect its small population. *Per capita*, it occupies the world's second and third positions for the number of publications and citations, respectively (Table 1). The citation input data show considerable variability among different fields (Table 2). Whereas in computer sciences Israel appears to rank first, and in chemistry, third, both with an impact 1.4-fold higher than the world average, in some other fields it ranks only 14-16th with a citation impact only 70-80% of the world average.

A similar impression is provided by Table 3, which compares data for Israel and the United States. In some fields, e.g., computer science or agriculture, Israel is on par with the United States in citation impact, in others, it is significantly lower. When normalized to the population size, however, the number of publications *per capita* in Israel is considerably higher than that in the U.S. for all fields, regardless of their citation impact, indicating that there is no direct correlation between the quantity of national publications and their quality. Table 4, column 5, shows Israel's ranking for the number of publications normalized to Gross National Product (GNP), rather than population. For most fields, Israel's ranking is very high, again with no correlation to citation impact.

The Immunology and Neurosciences Studies. The Division of Science undertook a more thorough evaluation of Israel's international standing in the fields of immunology and the neurosciences, in view of their relatively low ranking compared to other disciplines. Furthermore, they represent, respectively, a well-established discipline and a rapidly developing one. Finally, the contrast between their high bibliometric activity rankings (1-4th, normalized *per capita* or per GNP) and their low impact rankings (16th) was particularly puzzling (Table 4).

For this purpose, several additional evaluation parameters and strategies were employed:

1. "Steepness" of the curve measuring Israel's relative ranking
2. Comparison of Israel's ranking in different deciles
3. Time-dependent changes in the bibliometric data (5-year windows)
4. Comparison with individual Western countries (several methods)
5. Effect of clinical research on the citation impact
6. Normalization of data to the number of scientists in the field
7. Projections, based on the number of scientists in the various institutes of higher learning in Israel and their age groups (not completed due to lack of data)
8. Personal evaluations from respected world authorities in these fields.

Each criteria was designed to answer specific questions about Israel's world rankings and their significance. These are discussed individually in the sections that follow.

1. **How Meaningful is Israel's Exact Numerical Ranking?** The top histograms in Figure 1, although the names of individual countries are not legible, indicate

that Israel's exact position (arrow) in its rankings "neighborhood" is not all that critical. In immunology, the difference in the citation impact between Israel and the nine countries ranking immediately higher is not significant, given the accuracy of the method. (The charts at the bottom of the figure show that the percentage of publications in these two fields, out of the country's total publications, is relatively high in Israel compared to other countries, indicating that these fields are not underfunded or understaffed, compared to other fields, within the limits of the country's resources.)

2. **Is Israel a Quality Leader in These Fields?** A particularly important parameter from the point of view of the Academy is "excellence." This requires focusing on peaks of high quality research, rather than averages. One measure might be the normalized number of Israeli publications falling in the upper 1-2 deciles (upper 10-20%) of citation impact. A roughly equivalent measure is the ranking of Israel in specific deciles (Table 5). Israel's ranking varies little with decile, although it is slightly lower at the higher quality levels.
3. **How has Israel's Citation Impact Changed Over Time?** Graphs of Israel's citation impact from 1981 to 1995, averaged over overlapping 5-year windows (Figure 2), show that the absolute citation impact for immunology has remained rather constant, with only slight variations. In the neurosciences there was a steady increase, particularly over the last five years. Israel's *relative* impact (normalized to the world average) displayed a smaller increase in the neurosciences and suffered a slight decline in immunology. Still, on the whole, Israel has maintained a consistent position in these two disciplines over the last 15 years. Israel's share in the world's publications in the neurosciences

remained constant over this period, whereas in immunology there was a significant decline (Figure 3). This could indicate either diminishing Israeli emphasis on this field or a worldwide increase not matched by Israel.

4. **What are the World Trends Over the Same Period?** Time trends in citation impact and impact rankings for other countries are given for the 22 top-ranking countries in Tables 6, 7. Data are provided for the period as a whole and for its three consecutive 5-year segments. In immunology (Table 6), Switzerland and the U.S. remained the two top countries throughout all fifteen years. Some countries, e.g., Canada, rose in stature (from position 13 to 11 to 6) while others, e.g., Australia, declined (from position 3 to 6 to 12). Israel underwent a slight, perhaps non-significant, decline (from position 14 to 15 to 16). In the neurosciences, Israel has advanced in status from position 14 to 11 during the last 5-year period, while Sweden, for example, declined from rank 2 to rank 5. However, in the 5-year segments used, the absolute values for the citation impact are so small that minor differences can lead to unwarranted changes in rankings.

5. **Have Israel's Low Citation Ratings for Clinical Studies Skewed the Data?** The abundance of clinical research in the two fields studied, raised the question of whether the anomalously low citation ratings for Israeli clinical research could account for Israel's low ratings in these fields. However, as Figure 4 shows, the percentage of clinical papers in these two fields was not sufficiently high to have had a significant effect. Still, when clinically *oriented* publications (i.e., those with hospital affiliations) are deleted, Israel's citation impact in both immunology and neuroscience, while still lower than that of the leading countries, approaches the world average (Figure 5). That is, the

standing of Israel's *university* laboratory-based research seems compatible with world standards.

6. **What Happens When These Data are Normalized Per Scientist?** In judging the average productivity or quality of Israel's practicing immunological and neuroscience researchers, it is important to normalize citations, etc. to the number of practicing scientists, not the total population. Unfortunately it is often difficult to get accurate data on the number of scientists in particular fields in different countries. Some information, not particularly accurate, can be deduced from the number of members in the respective professional societies. The data, available only for immunology, are summarized in Table 8. In relative publication activity per immunologist, Israel ranked 7th by these measures, very close to Switzerland (6th), despite the wide gap in the citation impact between these two countries. One interpretation of these data could be that Israeli immunologists publish relatively low-impact papers at a relatively high rate. Stricter selectivity in training or funding might improve this situation.
7. **What can Israel Expect in the Future?** Projections to predict the status of these two fields in future years might be prepared using information on the number of scientists engaged in each field in Israel's universities, hospitals and research institutes, and their various age distributions. It could be particularly important to see if the research population is "aging." Unfortunately, such data was not readily available; and it was impossible to proceed.

8. **How do the Quantitative Indicator Studies Compare with Qualitative Expert Field Comments?** All the parameters and quantitative indicators considered to date are informative, but each has its own flaws. Hence, we also solicited qualitative field assessments from world-class expert scientists in these two fields, experts who were also familiar with Israeli science. Letters were sent to six or seven such authorities in each discipline (letter appended). Five responses in immunology and two in the neurosciences were received. Their essence is given below.

Immunology:

There is considerable consensus among the five assessments received, with most differences limited to nuance, style and terminology. All five respondents concurred that Israeli immunology has a long, rich tradition. During the 60s and 70s Israeli immunologists were among the world leaders, particularly in many fundamental areas. Chemical immunology at the Weizmann Institute had a major worldwide impact, mainly due to pioneering Israeli efforts and chemical mastery over the peptide synthesis needed to create new antigens.

At present, however, all respondents would describe the status of this discipline in Israel as "disappointingly fine" – fine compared to some other countries, but disappointing compared to expectations. It is basically competent, "with some true highlights from mid-career scientists, and some very promising younger scientists, but also a good deal of mediocre and some downright sloppy work."

Furthermore, Israeli immunologists have now largely abandoned the fundamental aspects of contemporary immunology, although a number of internationally recognized Israeli

immunologists still make original contributions and a "good showing" in selected areas (particularly in such applied areas as cancer immunology, autoimmunity and immuno-intervention). Little research of true distinction is being done in such basic areas as T-cell specificity, development, differentiation and function, or in molecular immunology. As one review put it: "too little energy is going into true scholarship in the best Jewish tradition."

In trying to account for these changes, the respondents contrast the tremendous increase in the number of immunologists worldwide (50-60 fold) during the last two decades, with the much smaller increase in Israel. In addition, modern immunology has become much more expensive and now requires enormous resources. Consequently, "young Israeli immunologists returning from highly successful postdoctoral experiences in world-class laboratories often find themselves with very limited access to the funds needed to undertake the kind of basic studies that could help to transform the [Israeli] immunologic enterprise."

There is considerable consensus that Israel urgently needs the emergence or recruitment of a charismatic figure to provide vigorous leadership and a sense of cohesion, and to galvanize interest in this important field. In addition, Israel needs to assure adequate resources to a cadre of talented young scientists, some to be repatriated from the best laboratories abroad, at least until their careers are launched and adequate funds are available from other sources.

Neurosciences:

Only two international experts responded to our request for evaluations. Furthermore, there are significant differences between the two replies received. The first reviewer regarded the neurosciences in Israel as first-rate, with an enviable international reputation. He was also impressed by the number of truly exceptional, highly gifted Israeli neuroscientists who are

actively pursuing research and training younger people. The breadth of Israeli interest is another strength: from the finest structure of molecular channels to the highest integrative brain functions, all the fields are represented by active and, in his view, brilliant participants. Considering that Israel is a small country, it is surprising that so much could be done so well, with no loss in quality. Compared to other small countries, Israel – in this view – is doing quite well.

In contrast, the second respondent detected somewhat of a decline in Israeli neuroscience over the last decade. Until ten years ago, Israel was superior to Austria and Switzerland, and on a par with France and Sweden (and perhaps, from 1960-1980, even with Germany); however – in this view – it is no longer at the cutting edge. Neurobiology changed radically in the early 1980s, with the development of single-channel research and the rise of molecular neurobiology, now a dominant theme in international neuroscience. Israel's cellular and molecular neurobiology has not kept pace with the rest of the world.

Both respondents agree that Israel is not currently a leader in molecular neurobiology, which is becoming increasingly important, although they differ on what Israel should do about it. The first respondent does not regard this as a disaster, as long as there is some representation in this area (as there indeed is) in all Israeli universities. This field is moving incredibly fast and is extremely expensive to pursue. Since Israel's financial resources are rather limited, taking a larger piece of the pie for molecular neurobiology would – in this view – be a mistake. Instead, Israel should promote other areas of expertise, which are truly original and have a distinct flavor of their own. In contrast, the second respondent feels that Israel should indeed try to keep up with the tremendous expansion of world interest in molecular

neurobiology. Furthermore, young scientists should change the focus of their research projects from short-term goals to a longer view, developing areas that will mature over time.

Summary and Recommendations:

It is interesting to compare the insights obtained from the quantitative indicators and the qualitative expert assessments. At their present state of development, quantitative indicators indeed "indicate" where to look, providing intriguing anomalies, concerns and hypotheses that should be further addressed by a wide variety of methods, including expert assessments. Our recommendations are based primarily on the latter.

Immunology:

1. The citation data indicate a slight decrease in the status of Israel over the last 15 years. This decrease is probably too small to be quantitatively significant; and even the relatively low rank of Israel in this discipline, compared to its ranking in other fields is also probably not a serious concern. For most high-ranking countries the actual spread in citation impact values is small. Israeli is *close* in citation impact to most European countries and surpasses Japan.

2. On the other hand, according to the evaluations of recognized international authorities in the field, there as indeed been a substantial decline in the global standing of Israel in this area since the 60s and 70s, when Israel had a major, worldwide impact on immunology. The citation indices do not cover that era, having been compiled only since 1981.

3. There is a shortage of good young Israeli immunologists.

4. As for the future, considering the recommendations of the experts consulted, Israel should encourage the development of areas in which we are wanting,

such as cellular and molecular immunology. We also need to attract several talented young immunologists, with excellent experience in world-class laboratories abroad, and offer them the academic positions and the resources required for high-quality basic research.

Neurosciences:

1. The bibliometric data show that the relative ranking of Israel for the period 1981-95, compared to its ranking in other fields, has remained comparatively low, although there has been a significant upward trend over the last five years. This is manifested not in its citation impact *per se*, but only in the relative ranking of Israel compared to other countries.

2. According to the evaluations of respected international authorities in the field, Israel exhibits excellence and leadership in several areas of neuroscience, but lacks strength in molecular neurobiology, one of the fastest growing fields.

3. There is disagreement, however, over whether a small country, such as Israel, can afford to compete internationally in such an expensive and fast-paced area, in which it is now weak, or whether the funds would be better spent pursuing excellence in a wider variety of areas in which excellence is more feasible.

4. As for the future, we concur with the experts' conclusion that we should continue to encourage and support Israeli neurosciences. In particular, young

scientists should be encouraged to enter the field and to focus on topics with long-term interest and potential.

Relative Impact of Various Fields of Israel Science (1998)
(Based on Bibliometric Data from 1981-1997)

Code	Field	Ranking
CSD	Computer Science	1
ECD	Economics & Business	2
EDD	Education	2
CHD	Chemistry	3
AGD	Agricultural Science	5
BID	Biology & Biochemistry	5
MBD	Molecular Biology & Genetics	5
MSD	Materials Science	5
PHD	Physics	5
SSD	Social Science	7
ASD	Astrophysics	8
OTD	Multidisciplinary	8
MCD	Microbiology	9
MTD	Mathematics	10
PLD	Plant & Animal	10
EVD	Ecology/Environment	11
EGD	Engineering	12
GED	Geoscience	13
IMD	Immunology	13
PMD	Pharmacology	14
PSD	Psychology	14
NED	Neuroscience	15
CLD	Clinical Medicine	17

Part II. Expert Committee Recommendations (1999)

Howard Hughes Medical Institu
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September 17, 1999

Professor Ruth Arnon
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Dear Ruth:

I have passed on to Bert and Torsten my revisions of Bert's excellent draft of our recommendations.

Cheers,

Eric R. Kandel, M.D.

ERK/mp
Enclosure

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Committee on Neurosciences

I. Introduction

1. It is the strong belief of the Committee that the Neurosciences represent a critical field of research for the future of Israel. To begin with most biologists believe that the biology of the brain, especially the biology of mental processes, represents one of the great challenges for science in the 21st century and a challenge that young scientists find particularly exciting and fulfilling. In addition, applied research in neuroscience is critical for the future of neurology and psychiatry, for the understanding of Alzheimer's disease, multiple sclerosis, Huntington's disease, Down's syndrome as well as schizophrenia and manic depressive illness. Finally, neuroscience also has a great economic potential related to the development of drugs that alleviate neurological and psychiatric disorders.

2. The Committee thinks highly of Israeli neurosciences. We think the rating of the Israeli neurosciences, as No. 16 on a global scale is completely inappropriate and disregards the areas of excellence in Israeli neurosciences. We think that is impossible to define the ranking in one single number.

3. The meeting of our Committee at the Israeli Academy provided a good opportunity to overview the field of neurosciences in Israeli in a more general manner. We are aware that an in-depth evaluation would require a much longer time (2-3 weeks) and a much more thorough investigation than we can provide. Therefore, this overview is incomplete and is based mostly on our personal experiences with Israeli neuroscientists at meetings such as the IBRO-meeting and on personal visits of Neuroscience Institutes in Jerusalem, Rehovot, Tel-Aviv, Haifa and Beer Sheba. All we can do in the time

available is to propose to the Academy the establishment of some guidelines for the next 10 years.

II. Recommendations

1. *Structural Changes in Neuroscience Research Departments*

a) We propose that each University should have an outside scientific advisory committee (SAC) to evaluate their activity in neurosciences and provide recommendations on a 3-5 year basis. The heads of the universities should have the power o implement these recommendations.

b) Since neuroscience offers not only great promise for solving problems that concern the general welfare but also offers extraordinary scientific challenges. We recommend that more faculty positions in the neurosciences should be established in relation to other fields, with a strong effort to rejuvenate and expand the faculty.

c) We urge the introduction of the aspect of competitiveness to faculty positions at the universities. This can be done perhaps by adapting the policy of rolling 5-year positions. This approach has proven highly successful at the EMBL. Alternatively, personnel, resources, and lab space might be allocated to individual researchers according to past performance judged for example by the SAC. We feel, however, that we do not sufficiently know Israeli society to recommend one particular scheme for introducing more competitiveness in allocating resources.

d) Neurosciences should be brought closer to other fields of basic science, namely by introduction of more interdisciplinarity into the neurosciences.

This is of particular importance for universities in which today there is often a physical separation on campus(es) between the neurosciences and other disciplines such as chemistry, physics and computer sciences.

e) Neurosciences at the universities should be enormously strengthened if the activities of different departments would be united campus-wide, as opposed to the current situation. For example at the Technion, neurosciences are part of the Medical School and located in town at a fair distance from all other faculties; at the Hebrew University two separate units for neurosciences operate in Ein Kerem and Givat Ram, respectively. At Tel-Aviv University, the Adams Center is only an umbrella with little actual leverage. Here all neuroscience departments should be united under one roof. An excellent example of interdisciplinarity and physical neighborhood is the Weizmann Institute. Here the neurosciences are brought together in two neighboring buildings connected by a bridge and they are in walking distance to Chemistry, Physics and Computer sciences.

2. Focus on Neuroscience Research Areas

a) Several Centers of Excellence already exist in a number of areas and should be even more strengthened. New Centers should be formed and areas of importance include:

- Understanding of the collective activity of neurons and neuron specific molecules. This area can be strengthened by promoting imaging techniques at all levels, including those necessary to observe cellular

signaling cascades towards those necessary to observe cell behavior in the context of the intact brains.

- Computational neurosciences – advantage should be taken of the high level of computer sciences research in Israel. Attract even more computer scientists for integration into the neurosciences.
- Cognitive neurosciences – expand and increase the computational aspect.
- Biophysics and neurophysiology, e.g. at present three are *foci* of excellent in Tel-Aviv University, Jerusalem, and at the Technion. This area in which Israeli labs were among the world leaders needs rejuvenation and should be expanded.

b) Windows of opportunity – areas in which there is no very high level presence of Israeli neurosciences or is in fact lacking:

- Developmental neurobiology.
- Animal models for human diseases, particularly those that can be generated by the use of regulatable knockout and knockin mice.
- Signal transduction. This field in general is of very high level in Israel in other areas, e.g. cancer research. It should be extended to the neurosciences.
- Clinical neurobiology. The research at present is too clinical and has to become more scientific by introducing basic science to clinical research.

3. *Improvement of Infrastructure*

Neuroscience has become more and more interdisciplinary and required high-tech equipment that cannot be installed in all universities.

- Specific items of state of the art equipment which are not easily available in Israel and are essential for high level research should be purchased. For example, facilitation for construction, raising and maintenance of genetically modified animals (K.O. and K.I. technology); two photon excitation microscopy, fMRI dedicated to basic research.
- As an independent issue, it is recommended that all activity on neurosciences is performed at one location in each university, so that more sophisticated equipment that already exists in other faculties (Physics, Chemistry) will be available to the neurobiologists. For example, in Haifa, the Rappaport Institute, and the Technion could get together in the development instrumentation of cutting edge equipment for cell and *in vivo* brain imaging using infrared, multi-electrode recording, SQUID technology in conjunction with cognitive neurosciences.

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To: Israel Academy of Sciences and Humanities

From: Herman N. Eisen
Fritz Melchers

We are pleased to submit the enclosed report on the status of research in immunology in Israel. The report was prepared at the request of Prof. Ruth Arnon. If you wish to discuss any issues or questions about the report please do not hesitate to communicate with us..

Research in Immunology in Israel: A Brief Overview

submitted to

Israel Academy of Sciences and Humanities

by

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September 14, 1999

Research in Immunology in Israel: An Overview

In this report we address a series of questions put before us by Prof. Ruth Arnon, Chairperson for the Sciences, the Israeli Academy of Sciences and Humanities. The questions concern the current status of research in Immunology in Israel, relative to other countries, and possible changes in this status over the past approximately 15 yrs.

To address these issues we looked at summaries of recent research activities and publications from about 70 investigators at the Weizmann Institute, the Tel Aviv Faculty of Sciences, and the Hebrew University Medical School and its Lautenberg Center. Investigators at the Tel Aviv Medical School were not considered. Owing to their acknowledged status and seniority and we also omitted Prof. Michael Sela and Prof. Ruth Arnon from consideration.

Bibliometric data from the US-based Institue for Scientific Information,based on papers published since 1981, indicate that in terms of the number of papers published in Immunology, ranked by country, Israel was 16th, just ahead of Finland and Italy, but when normalized for population size, it ranked in the top three (along with Switzerland and Sweden). When the rankings were based on the "impact" of publications, judged from the frequency with which published papers are cited in other publications, Israel's position was 14th, and when normalized for population it was 3rd, well behind Switzerland and Sweden, but closely bunched with Denmark and the US. Before considering the significance of these rankings it must be emphasized that there are widespread misgivings about attempts to quantify the significance of scientific reports from the frequency with which they are cited. Thus, for example, one of the most highly cited papers on record describes a minor improvement in a colorimetric assay to measure protein concentrations. With this limitation in mind, we proceed, nevertheless, to accept the view that Israel may indeed rank around 14th in terms of the impact of its Immunology publications. Since several other scientific fields in Israel rank considerably higher, one is led to wonder why Immunology in Israel does not enjoy a higher ranking? Is the current ranking acceptable? What can or should be done about it, if anything?

In addressing these questions we want first to call attention to the great changes that have taken place over the past 15-20 yrs in immunological research. Early on, Immunology focused primarily on seeking explanations for major immunolgical phenomena, such as the specificity and structure of antibodies, using special techniques and analytical methods developed by and for immunology. As a result, except for some notable applications of organic and protein chemistry and genetics, Immunology was largely isolated from other biological and biochemical disciplines. Over the past 10-15 yrs, however, the concepts and tools of diverse biological disciplines have been introduced to analyze previously unexplored, fundamental aspects of the immune system, involving the differentiation and development of immune cells and the signaling cascades that lead to tremendous cellular amplification systems set off by ligand-binding to antigen-specific receptors on lymphocytes to trigger the genes involved in controlling cell division, differentiation, and the production of a large number of potent effector molecules (cytokines). These newer approaches have also resulted in expanded opportunities to probe more effectively the

more traditional problems in antigen-recognition, the pathogenesis and control of autoimmune diseases and the development of vaccine strategies against major infectious disease for which current vaccines are not available or inadequate (AIDS, tuberculosis, malaria). Most significantly, there has occurred over this period an enormous increase in the number of investigators world wide, especially in the American-European community. Thus, a conference a few years ago on the highly restricted topic of the T cell receptor had to be limited to around 650 investigators, and international conferences now draw around 10,000 or more investigators.

Given the wide-ranging magnitude and pace of immunological research world wide, it is rather remarkable that the immunological community in Israel, which has expanded less over this time, fares as well as it does. That it does so is a tribute to the intelligence, energy, skills and spirit of Israeli immunologists as a group. Another general source of strength derives from the prevailing intellectual climate, especially in computer and physical sciences and mathematics. We note that peptide synthesis, developed at the Weizmann Institute around 30 yrs ago, has a momentum that still carries on and promises to result in a new form of therapy for a major source of human morbidity, the autoimmune diseases. Finally, we believe that judging from the number of papers Israeli immunologists publish in the better journals, around one-third of these investigators are fully competitive in the sense that were they free to apply on an equal footing for grants from US or European agencies, they would likely be successfully. Nevertheless, we perceive some serious problems that burden immunologists in Israel more than in the most productive segments of the American-European community. By emphasizing these problems below we hope that efforts to deal with them may improve conditions and enhance the scientific productivity of our Israeli colleagues.

Sources of concern

1. **Recombinant DNA technology.** This technology has transformed research in Immunology, as it has the rest of biomedical research. The ability to produce recombinant proteins of importance (e.g., T cell receptors, MHC molecules) and to generate cells with new properties by introducing genes into them, and to create new strains of mice having specific genes deleted or new ones introduced, have created research opportunities hardly dreamt of 10 yrs ago. A cursory glance at a current issue of a first grade immunological journal (IMMUNITY, July, 1999) shows, for example, that 9 out of 10 papers made use of or depended entirely on this technology. Yet, we have the impression that it was late in coming to Israeli immunologists, and even now is not vigorously represented. Those few who are skilled in its use do indeed manage to have their papers published in the best journals (see below).

2. **Journals.** A relatively very small proportion of Israeli publications in Immunology appear in the most prestigious journals--Nature, Science, Cell, Immunity, J.Exp Med or PNAS. Many appear instead in less widely read "specialty" journals , perhaps because of the tendency to publish short papers, rather than more information-dense papers. This problem is probably related in part to the tenure track issue discussed below.

3. **Funds.** We estimate from the number and average size of grants awarded by the Israeli Academy, the German-Israeli Fund , and the Binational US-Israeli Fund, that an Israeli immunologist who succeeds in competing for all three is likely to secure funding of maximally about 150,000$ per yr. This amount is what a barely viable lab is likely to have in the US, and is substantially less than the average well established investigator would receive in the US or in a well established Institute like the Basel Institute for Immunology. If research productivity were somehow normalized for the funds expended per investigator, Immunology in Israel would almost certainly rank much higher, perhaps near the top, world-

5. The development of tenure-track scientists. In the US (but perhaps less so in many parts of Europe) there is a general conviction that much of the best science emanates from young investigators who function entirely independently and are free to pursue their own research agendas. Moreover, they normally have around a 5-yr period before being evaluated for tenure level appointment. Many argue this period should be a bit longer, long enough, ideally, for scientists not to feel pressured into engaging in short term, low-risk research that leads to many papers, but is not conducive to taking risks on potentially highly rewarding, more original research ventures. We have the impression that with our young Israeli colleagues the time-to-decision is much shorter (3yrs?). This may account for their tendency to publish many papers is less than first-rate journals, a recipe for low impact science!

6. Pool of new talent. The vigor of a scientific discipline is often reflected by the number of students seeking to enter it. We have the impression that graduate programs in Immunology are not attracting large numbers of Israeli applicants. Of course, the size of the Israeli population may account for the problem in part. It is also possible that students perceive greater career and job opportunities in other fields of science, such as computer science, than in Immunology, where job opportunities are pretty much limited to academic institutions. Or it may be that young students in Israel do not see Immunology as an intellectually challenging field.

Recommendations

It could be argued that the status of Immunology in Israel is acceptable, and that no drastic or special efforts be made to significantly strengthen it. We hope this view will not prevail, for it seems likely that if steps are not taken to improve matters we are likely to see a declining status of this field in Israel. We believe this to be the case, because in the American-European community this field is attracting increasingly strong support from funding agencies and from the pharmaceutical and biotechnology industries. In some measure, the AIDS pandemic is a driving force, with the US now spending well over a billion (10exp9) dollars a year on AIDS research alone, much of it on basic Immunology. Besides its significance for AIDS and many other medicine problems, the immune system is attracting attention from basic molecular and cell biologists, because immune cells are such accessible and tractable material for studying general problems in development, differentiation, signal transduction, programmed cell death, etc,.--and at the same time the relevance of these basic problems to practical applications in medicine is often obvious.

When it comes down to specific recommendations, however, we see only limited possibilities. Its easier to identify problems than to offer practical solutions. Nevertheless, we offer the following suggestions:

1) Promote activities in areas that are not yet well represented world wide in Immunology. The obvious examples here are bioinformatics and computational biology. With the genomic projects now underway, an enormous amount of new information is being rapidly accumulated, and the existing community of immunologists is hardly equipped to mine its potential wealth. These activities would also allow Israeli immunologists to take advantage of the great strengths of computer science and mathematics in Israel.

2) Modify the tenure track system by making a strong effort to identify talented investigators at an early age and to insure that they enjoy real independence in developing their individual research agendas, especially allowing them more time before tenure decisions--say 5-6 yrs, instead of 3 yrs, which is what we understand in currently the common practice. With a longer time they would be under less pressure to tackle projects that entail little risk and are sure to result in many papers, albeit brief ones in second-rate journals. Instead, the longer time might well encourage investments in projects with potentially greater rewards.

3)Recombinant DNA technology should be promoted vigorously, using workshops or other means. Without having the basic skills and experimental fluency in this area its hard to see how young investigators can hope to compete with the best immunology elsewhere.

4) Encourage interdisciplinary collaborations with colleagues in related sciences in Israel and abroad. Immunologists clustered in their own department run the risk of becoming isolated from other scientific colleagues and thereby losing opportunities for infusions of new ideas and techniques. An example is the Department of Biology at MIT. It encompasses a wide range of biological disciplines without borders. It gains greatly in vigor and dynamism by not being divided-- as it would be if it were in a typical American medical school,-- into separate departments of Biochemistry, Microbiology, Anatomy, Physiology, Pharmacology, etc.

5) Increased financial support is definitely needed. The modern technologies that drive research in the genetic, molecular, and cellular bases of immune systems are very costly. It may be that if, say, one-third of the suboptimally performing investigators were no longer supported, a considerable amount of resources would be freed up to increase support for others. External reviewers (i.e., foreign?) might help in this situation as they might find it easier to be objective than members of the Israeli community.

We hope the foregoing comments are of some value. It was a pleasure to meet and exchange ideas with Israeli colleagues We especially wish to express our gratitude to Prof . Arnon for making our visit so pleasant. Her solicitude and organizational skills helped greatly to make our short visit a pleasure rather than a burden.

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