

# The American Pain Society and Translational Pain Research

*A position statement from the American Pain Society*

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## **Purpose**

The American Pain Society (APS) offers this statement in an effort to identify obstacles to translational pain research and provide possible solutions, list gaps in existing basic and clinical pain-related research, and describe how translational pain research might fit in the National Institutes of Health (NIH) Roadmap.

## **Definitions**

The term “translational research” is used by the NIH to describe the laudable goal of translating scientific discovery into practical applications. For translational research to be successful, basic and clinical scientists must work together to advance the understanding and treatment of disease processes and symptoms. The APS mission is to embrace these ideals to facilitate interdisciplinary, translational research. Translational pain research involves bringing together basic and clinical scientists to study diverse aspects of pain using biomedical and social science tools with the goal of moving laboratory research to the clinic and clinical insights into the laboratory. This research is expected to lead to improved symptom control. Painful diseases afflict millions of Americans daily, and pain motivates these individuals to enter the healthcare system. Any research that could alleviate pain by moving findings from the bench to human testing and then to the bedside would have immediate and profound benefits. To date, the translation from scientific discovery to successful clinical pain management intervention has been slow. This report identifies several steps that could speed up the translation.

## **Obstacles to Translational Pain Research**

There are numerous obstacles that stand in the way of translational activities. Inadequate funding is an obvious impediment. Only 1%–2% of research funded by the NIH has relevance to pain, a symptom experienced by 100% of Americans in their lifetimes (Bradshaw, Nakamura, & Chapman, 2005). One reason for a disparity between the clinical significance of and funding for a pain-relevant discovery may be a perception that pain-related research is inadequately mechanism-driven. Symptom-based diseases with pain that is out of proportion to the observed pathology is a clinical reality that, at present, is difficult to reconcile with our scientific culture of precise linkage of measures. Junior faculty who pursue clinically-relevant activities may find themselves going against the culture of their own institutions and may not be professionally rewarded. Similarly, study sections immersed in the same culture may not be enthusiastic in their support for pain-related studies. In these times of highly competitive funding, applications need to be both methodologically sound and championed by reviewers that recognize the profound clinical value. Treatment- and symptom-based research has struggled to find champions. Increasing the presence of individuals on review committees with expertise related to clinical pain will ensure that clinically-relevant applications receive fair representation. Preliminary data that reinforces the validity of methods and the likelihood of success is necessary for competitive grant applications. Governmental, industrial, and nonprofit organizations dedicated to the treatment of painful diseases need to step forward and provide the seed grants that allow for the formation of competitive programmatic pain research endeavors.

Presently, interactions between clinicians and researchers are inadequate. Formal training opportunities for new clinicians to learn laboratory methods (e.g., training grants, K-awards) have to compete with the financial rewards of clinical practice. Organized medicine should assist with salary disparities that discourage young clinicians from entering a research career. Programs to facilitate the training of laboratory-based scientists in clinical methods are uncommon. The creation of incentives for cross-training of both new and mature faculty through changes in funding

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and institutional policies would likely have a favorable cost-benefit return given the dedication of basic scientists to continuing academic activities and the ability of more senior clinicians who are confident in their clinical skills to branch out into research activities.

There is a lack of infrastructure at many institutions to assist researchers through regulatory and monitoring agencies that are necessary for the protection of experimental subjects and scientific integrity. Development of a researcher-friendly environment within regulatory agencies (e.g., FDA) would move forward the implementation of basic science discovery without the need for industrial sponsorship and its resultant intellectual property issues. Regulatory obstacles and expense issues also serve to slow multicenter trials that could allow for a rapid generation of data with sufficient statistical power to definitively determine responses to therapies. Creation of an infrastructure that could link multiple sites and provide necessary statistical and administrative support would encourage the development of such studies. Some models of such cooperative efforts are the oncology-related networks; emulation of those networks could lead to greater treatment options and outcome measures relevant to pain management. Key factors that have allowed the field of oncology to move forward significantly are: (1) the recognition that translational research is interdisciplinary and beyond the borders of departments and institutions, (2) the existence of infrastructure for oncology centers that facilitate translational research and make such efforts productive and successful, (3) the allocation of research funds to support the growth of oncology research centers, and (4) the creation of an NIH institute that serves all aspects of oncologic research both on an intramural and extramural level.

### **Opportunities in Translational Pain Research**

There are areas in need of improvement within current pain-related research. Our preclinical models of types of pain often differ from models of painful diseases, and, therefore, interpretation of the results may be limited. As pain is both a sensory and emotional experience, our models need to reflect subtle differences in pain processing and pain-evoked responses. A necessary comparison to the human animal is needed when developing systems in nonhuman animals. Experimental models require responses to be consistent and robust in order to be reliable, but these responses prove to be at odds with clinical results where the magnitude of pathology and symptomatology are often mismatched. Laboratory-based scientists may need to consider studying outliers rather than excluding them.

Whereas many painful diseases are life-long, our studies and models are not. It has been postulated that chronic pain should no longer be considered a disease symptom, but rather a disease in its own right (Niv & Devor, 2004). A significant gap in both basic and clinical research is that the researchers have been limited to relatively short-term studies of both the generation of pain and the clinical treatments for pain. Important questions related to remodeling of neurocircuitry, adaptations to pain, and the long-term benefits of interventions are still left unanswered. Studies with extended timeframes are expensive and often made difficult by regulatory requirements. There is an urgent need for the development of greater infrastructure in this area to serve multiple purposes. Databases, registries, and tissue banks similar to those utilized in oncological research could be developed and would allow for the probing of clinically relevant questions related to specific diseases and comorbidities over extended time periods.

### **Improving Translational Pain Research**

An important stimulus that would increase successful translational pain research is the development of infrastructure at both local and national levels. The NIH Roadmap seeks to develop such infrastructures, and pain-related research could serve as an exemplar for such efforts. Pain research is interdisciplinary and can address needs related to multiple disease processes. It is translational in that the goal of pain-related research has always been the development of practical applications that lead to pain relief. It has been disappointing that the pain-related portfolios of the multiple institutes of the NIH have progressively dwindled. Multi-institute support for infrastructure related to pain research is imperative and multi-institute support of pain-related investigations must be enhanced if we are to move toward the translation from discovery to practice. It is time for the public to ask policy makers to

**Table 1. Translational Pain Research Problems and Suggested Solutions**

<b>Obstacles</b>	<b>What NIH can do</b>	<b>What APS and other organizations and institutions can do</b>
Undervaluing of the clinical significance of pain mechanisms and treatment	<p>Change policy to increase weighting of significance (consider a separate score)</p> <p>Increase expertise and enthusiasm related to pain on review panels</p>	<p>Increase public awareness of the value of pain-related research</p> <p>Encourage the public to express interest in pain research to elected officials</p>
Inadequate clinician-researcher interactions	<p>Provide training opportunities for basic science researchers to learn clinical methods and endpoints</p> <p>Provide training opportunities for established clinicians to learn basic science methods</p>	<p>Increase social and professional interactions at regional and national meetings of organizations related to painful diseases</p> <p>Assist with mid-career interactions through funding and coordination</p> <p>Increase awareness of reverse translation (bedside to bench)</p>
Inadequate funding for pain research	<p>Increase funding of exploratory grants, training grants, and researcher-initiated grants through program announcements and request for applications</p> <p>Encourage individual institutes to have pain portfolios that reflect the importance of pain in their diseases of interest</p> <p>Revise the review process related to clinical significance</p>	<p>Encourage financial support by funding organizations related to painful diseases</p> <p>Increase access to seed grants</p>
Inadequate incentive for junior faculty to pursue pain research	<p>Increase funding of exploratory and training grants</p> <p>Make indirect costs of K-awards more consistent with other awards</p>	<p>Change the culture of the scientific community to reward research with high clinical significance</p> <p>Provide supplemental funding to national awards to limit salary disparities</p>
Burdensome regulatory issues	<p>Create national and regional advisory services to assist pain researchers</p> <p>Liaison with regulatory agencies to form research-friendly environment</p>	<p>Create local, regional, and institutional advisory services to assist researchers with regulatory issues</p> <p>Sponsor short courses and symposia to assist with training about regulatory issues</p>
Inadequate multicenter coordinating infrastructure	Establish multicenter coordinating infrastructure through formation of institute or multi-institute collaborative effort with dedicated resources	Assist in establishment of clinical networks
Inadequate access for researchers to clinical databases or tissues	Establish central registries, data bases, and tissue banks related to pain	Encourage local interactions that allow sharing of information and tissues

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respond to an obvious human need with real and effective support. It is also time for nongovernmental organizations dedicated to painful diseases to support seed grants, laboratory-clinician interactions, and infrastructure that would allow more investigators to dedicate themselves to projects that they—and the public—believe to be important. Some research obstacles are listed in **Table 1** as well as suggestions for solutions that would need to be implemented by the NIH, APS, national organizations, local institutions, and individual members of all these groups. This is a beginning that will need to be expanded and improved upon by all participants.

## References

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