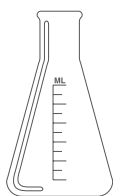


Biopharmaceutical Section



American Statistical Association

Biopharmaceutical Report

Volume 14, No. 3

Fall 2006

Chair: Stacy Lindborg

Editors: Richard Caplan, Philip Pichotta

Note from the Editors

In this issue we are pleased to publish the third article on biomarkers, written by Philip Iversen and Ann Cleverley. Thank you, Philip and Ann, for your contribution and patience. Together with the two articles in our last issue, we have a good overview to biomarkers.

Many past issues of the *Biopharmaceutical Report* have included one long feature article. Some issues comprise smaller articles. If you have a strong preference for one format or another, let us know. We always aim to bring timely, useful information to the membership, and we are progressing towards a more regular publication schedule. There is a "Let's Hear from You!" note at the end of the newsletter, and we mean it. If you have preferences about the composition of the newsletter; if you have suggestions for articles; if you want to write an article; if you have an announcement that would be of interest to other members in the section; then the editors are easy to contact. ■

Letter from the Chair

Stacy Lindborg

It's hard to believe that another year has almost passed us. As we move into fall 2006, two key meetings for the Biopharmaceutical Section have passed us and now are a part of our history, the Joint Statistics Meetings and the FDA/Industry Workshop.

The Joint Statistics Meetings (JSM) were held in Seattle, Washington, August 6–10, and focused on the theme "Statistics for an Uncertain World: Meeting Global Challenges." The Biopharmaceutical Section once again had a clear and strong contribution to the

breadth of the overall program with 40 Sessions: 7 invited sessions, 13 topic contributed sessions, and 20 contributed paper sessions. Biopharmaceutical Section members also led 34 round table luncheons.

Biopharmaceutical Section awards were once again given at the Business meeting. Awards for the best contributed paper from the JSM 2005 meetings resulted in the naming of the following (listed from

Contents

Featured Articles

Development of a biomarker for use in early clinical trials—a specific example <i>Philip Iversen and Ann Cleverly, Eli Lilly and Company</i>	3
ENAR 2007 <i>Ann Herring</i>	8
A New Journal! <i>Statistics in Biopharmaceutical Research</i> <i>Joe Heyse</i>	9

Biopharmaceutical Section News

Note from the Editors	1
Letter from the Chair <i>Stacy Lindborg</i>	1
Roundtable sessions at the Joint Statistical Meetings <i>Amit Bhattacharyya</i>	10

first to third place): Devan Mehrotra (Merck), Alex Dmitrienko (Eli Lilly & Co.), and Craig Mallinckrodt (Eli Lilly & Co.) The student paper awards illustrated

My first goal was to continue to diversify programs sponsored by our section to better serve our broad membership.

a strong set of manuscripts from a diverse set of universities. The winner was Hongying Dai, University of Kentucky with a paper on the topic “Omnibus testing and Gene Filtration in Microarray Data analysis”. Honorable mention awards were given to David Lewin, University of Pennsylvania on the topic “Using Instrumental Variables to Improve Safety Estimates from Clinical Trials” and Melissa Spann, Baylor University on the

topic “Bayesian Adaptive Non-Inferiority and Safety Assessment Retrospective Analysis of Clinical Data”. Congratulations to all the award winners.

There are many people to thank for the success of the Biopharmaceutical Section and events of the JSM program including B. Christine Clark (ICON Clinical Research), program chair; Amit Bhattacharyya (GlaxoSmithKline), program chair-elect; Shuguang Huang (Eli Lilly & Co.), contributed paper chair; and Student paper committee: Aparna Raychaudhuri (Centocor, R&D), chair and committee members Lei Zhu (GlaxoSmithKline), Xiaohua Zhang (Merck), Jennifer Gauvin (GlaxoSmithKline), Lilianne Kim (Centocor, R&D), Margaret Minkwitz (AstraZeneca).

The 10th annual FDA/Industry Workshop was held in Washington D.C., September 27–29 and focused on the theme “Statistics in the FDA and Industry: Past, Present, and Future”. The meeting had record attendance much to the success of the program and its organizers. Lee Kaiser (Genentech) and Richard Kotz (FDA/CDRH) played key roles heading up the steering committee. Special thanks are given to Katheleen Wert for her hard work and planning, which resulted in an efficiently run meeting. For a complete list of planning committee members, see the program on the Biopharmaceutical website: <http://www.amstat.org/meetings/fdaworkshop/pdfs/2006FDAProgramIntroduction.pdf>. Next year the roles of co-chair will be passed

to Dionne Price (FDA/CDER) and Matilde Sanchez (Merck). If you have interest in suggesting topics or willingness to volunteer please contact them directly.

We are getting fairly regular requests to co-sponsor and advertise for other professional organizations (e.g., ENAR, DIA) and sections. I take this as a sign of the health of our Section and the impact of our members through our organizations. We will continue to bring information that we feel is useful to our membership but will use appropriate routes of communication (e.g., opting for notices in the *Biopharmaceutical Report* versus use of our email distribution list).

The arrival of fall also signifies that I will soon pass the “Letter from the Chair” pen to Brian Wiens (Myogen, Inc.) as he prepares to assume Section Chair for the Biopharmaceutical Section. Along with Brian, I would like to welcome a host of talented individuals to new and continued roles on the Executive Committee. Serving alongside Brian include: Kannan Natarajan (Novartis), chair-elect; Devon Mehrotra (Merck), secretary 2007–2008; Mani Lakshminarayanan (Pfizer), treasurer 2005–2007; Amit Bhattacharyya (GlaxoSmithKline), program chair; Kalyan Ghosh (Merck), program chair-elect, Neal Thomas (Pfizer), publications officer 2007–2009; Council of Section representatives Naitee Ting (Pfizer), Anna Nevius (FDA/CVM), and Margaret Minkwitz (AstraZeneca); and last but certainly not least our editorial staff for the *Biopharmaceutical Report*: Philip Pichotta (Statistical Consultant), editor; Richard Caplan (AstraZeneca), past-editor; and Tom Dobbins (Merck), editor-elect.

I’d also like to thank all of the dedicated members of the Biopharmaceutical Section who have selflessly volunteered hours to ensure our Section could deliver another successful year. Professional societies and sections such as ours simply cannot survive without dedicated individuals to keep the service to members and programs alive. As in the past decade, the role of professional societies will continue to evolve. It is crucial that the leaders of the Section continue to ask what evolving role the Section should play for the members they serve. It is also vital that Section members continue to ask ourselves and discuss with our colleagues the question “Do I need the American Statistical Association and should I be a member of the Biopharmaceutical Section?” It is equally important that the answer be “yes!” to both. Please feel empowered to bring your suggestions to any member of the Executive Committee at any time and choose to get more involved in the Section.

As I reflect on the impact I hoped to help create through our Section I am pleased to provide an update. My first goal was to continue to diversify programs sponsored by our Section to better serve our broad membership. Appointments to the Executive committee brought expanded device and biologic membership to the group. In May, the Section helped organize a discussion at the Midwest Biopharmaceutical Statistics workshop for a group of statisticians focused on animal health biologics. We are hopeful that this discussion will lead to future engagement with the Section. Earlier this year, through the leadership of Greg Campbell, the ASA Board of directors approved the creation of a Special Interest Group on Devices, under the Biopharmaceutical Section. The

Section has seen the continued strong presence of topics related to devices on Biopharmaceutical programs and hopes it will continue.

The second goal was to challenge the way we view our continued healthy budget and consider exciting new ways to reach out to our broad membership. I am pleased to report that at the upcoming executive committee transition meeting in November we will review a number of proposals discussed in August and finalize proposals for short-term actions. Watch for upcoming communications.

In closing, it has been an exciting year with many exciting initiatives in progress. I look forward to working with Brian and the rest of the Executive Committee as we move into 2007. ■

Development of a Biomarker for Use in Early Clinical Trials

A Specific Example

Philip Iversen and Ann Cleverly, Eli Lilly and Company

Overview

Clinicians have used biomarkers to monitor therapeutic benefit and disease progression in patients for many years. What is reasonably new is the formal use of biomarkers in early phase drug development and this is particularly true of the use of translational biomarkers; biomarkers that can be used in both pre-clinical and clinical studies.

The National Institute of Health¹ working group's definition of a biomarker is: "a characteristic that is objectively measured and evaluated as an indicator of normal biologic processes, pathogenic processes or a pharmacologic response to a therapeutic intervention."¹ A clinical endpoint is defined as: "a characteristic that reflects how a patient feels, functions or survives" and a surrogate endpoint is a "biomarker intended to substitute for a clinical endpoint". Relatively few biomarkers have become recognized as

surrogate endpoints for drug approval, which is not to negate the value of biomarkers in drug development.

Baker² lists types of biomarkers:

- a** disease—indicating the presence of a particular disease;
- b** Efficacy or outcome—correlates with the desired effect of a treatment, but not intended as a substitute for a clinical endpoint as in surrogate endpoints;
- c** mechanism—suggests a drug affects the desired pathway;
- d** pharmacodynamic—used in early clinical trials to determine the dose that has the highest response;
- e** target—shows that a drug interacts with a particular target, e.g. PET imaging;

- f toxicity—indicate potentially harmful effects and
- g bridging or translational—may be related to disease, efficacy and/or toxicity.

These are useful to keep in mind when distinguishing between what is used where, when and why.

There is currently much research activity within the various 'omics (genomics, proteomics, metabolomics) fields that are investigating ways in which we can identify likely biomarkers that will be useful for different purposes. Potential biomarkers can also be identified by prior knowledge of what is involved in the signaling pathway that a particular compound is designed to impact.

This article describes the pre-clinical development of one protein as a specific biomarker and its early transition to use in clinical trials. This protein is known to be involved in a signaling pathway affecting cancer cell behavior. This biomarker can be considered as both a translational and a mechanism biomarker.

Scientific Rationale for the Choice of Biomarker

The multi-functional cytokine transforming growth factor- β (TGF- β) is a member of a large family of growth factors involved in the regulation of a diverse array of biological processes including cell growth and differentiation, matrix modulation, and embryonic development. Cell surface binding of the TGF- β ligand leads to the formation of a heteromeric complex involving type I (T β R-I) and type II (T β R-II) receptors, each of which are transmembrane-spanning proteins featuring a serine/threonine kinase domain. Downstream signal transduction is mediated by the T β R-I kinase domain through the phosphorylation of Smad proteins, which as oligomeric complexes translocate to the nucleus and regulate gene response via association with DNA transcription factors.³ The TGF- β signaling pathway may play a role in a number of disease states involving inflammation, angiogenesis, and immune function, including fibrosis,⁴ wound healing,⁵ Alzheimer's disease,⁶ atherosclerosis,⁷ hypertension,⁸ restenosis,⁹ and cancer.¹⁰

Pre-clinical development of an oncology drug candidate focused on defining the PK/PD relation-

ship in vivo for inhibition of TGF- β signaling as determined by phospho-Smad (pSmad) modulation in xenografted human tumors in mice and rats.¹¹ The optimal dose and schedule was then utilized in three pre-clinical mouse models of tumor growth inhibition to demonstrate that the candidate had anti-tumor activity. Clinical development, which is ongoing, will incorporate pSmad modulation as a means to confirm the mechanism of action of the compound. Although select patients will undergo pre- and post-treatment biopsies to evaluate target modulation in tumor tissue, peripheral blood mononuclear cells (PBMCs) were investigated as a surrogate tissue for routine evaluation of target modulation in vivo. The TGF- β signaling pathway is illustrated in Figure 1.

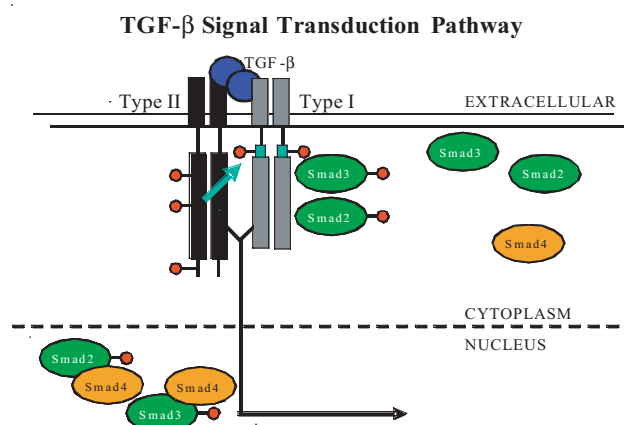


Figure 1
Diagram of TGF- β receptors (Type I and Type II) and the downstream signaling cascade that begins with the Smad proteins.

Pre-clinical Development of the Biomarker Assay

A pre-clinical biomarker assay was developed using a Western blot method to detect pSmad and total Smad protein (tSmad), using standard procedures. Since the expression level of Smad (tSMAD) dictates the extent of phosphorylation observed (pSMAD) in the ex vivo TGF- β stimulation procedure, total Smad was measured to allow data normalization. Smad levels were measured in tumor tissue from mice and rats, and in PBMCs from rats and human donors. The animal studies used human tumor xenografts following standard protocols. The goal was to be able to routinely use blood samples rather than tumor biopsies in humans. For the clinical trials, the Western blot assay

was converted to an ELISA assay because the ELISA was more quantitative, easier to validate clinically, and had logistical advantages.

Statistical Analysis

In a Western blot assay, each sample is tested in a separate lane on a gel. In each lane, dark bands appear that indicate the presence and amount of different proteins, as illustrated in Figure 2. A control lane was used to identify each band with its corresponding pro-

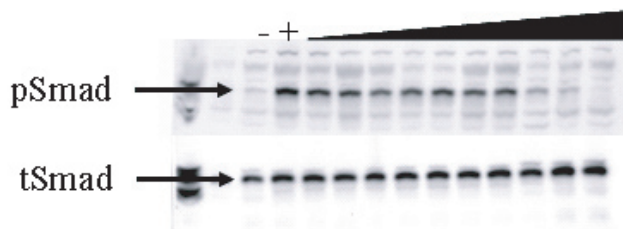


Figure 2
Example Western blot gel from the human donor experiment. Columns labeled – and + are controls while the triangle indicates increasing dose of drug.

tein, and the protein of interest was quantified via its intensity. Total Smad was measured in samples from the same subjects but was detected on different gels from pSmad, since the detection intensities between pSmad and tSmad were different. There were 12 lanes per gel. In the animal experiments, different samples from the same experiment were tested on different gels. To account for possible gel effects, samples from the vehicle control animals were tested on every gel. Between gel effects were found to be minimal, in general. In the human donor experiment, each subject's sample was divided into 12 aliquots. Two were used for controls (+ or – TGFβ stimulation). The other 10 were used for a 10-point dose response starting at 20 μM with 3-fold dilutions. PSmad and tSmad were measured in each aliquot. Figure 2 shows an example gel.

The questions to be answered from the pre-clinical experiments were:

- 1 How to normalize pSmad to tSmad?
- 2 Does the candidate inhibit the pSmad signal similarly in each species?
- 3 Is tumor inhibition similar to PBMC inhibition?

- 4 Does the ELISA give similar results compared to the Western blot?

1 Normalizing pSmad to tSmad

Several options were considered for normalization. These included no normalization, a ratio of pSmad to tSmad, and an adjusted ratio based on analysis of covariance (ANCOVA). In the log scale, we used this ANCOVA model:

$$y = \beta_0 + \beta_1 x + \theta_i + e$$

where $y = \text{Log}(\text{pSmad})$, $x = \text{Log}(\text{tSmad})$, and θ_i is the treatment effect. Rearranging,

$$y - \beta_1 x = \log\left(\frac{P}{T^{\beta_1}}\right) = \beta_0 + \theta_i + e$$

Thus, the ANCOVA is the same as an ANOVA on the log transformed, normalized response, P/T^{β_1} . If $\beta_1 = 1$, we have the typical ratio normalization. It is important when using this type of normalization that the treatment does not affect the covariate, tSmad. In our case, the data satisfied this requirement as there was no evidence of differences between β_1 estimates across a range of doses, including comparison with the control group. Because of sub-sampling in the human donor experiment, we added a random effect for subjects to the model.

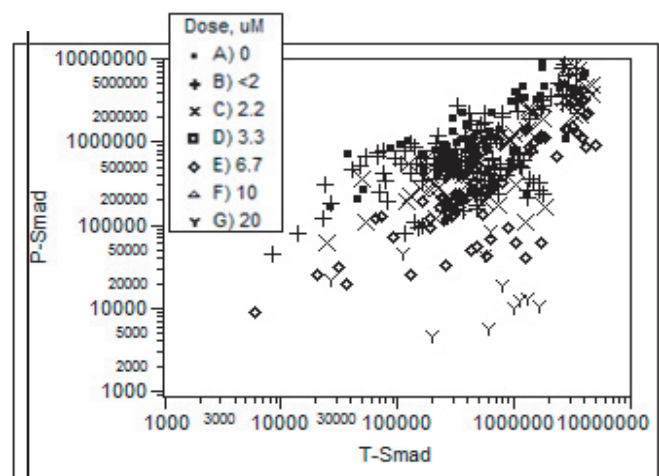


Figure 3
PSmad vs. tSmad by dose group for the human donor experiment.

Figure 3 shows an example plot of the human donor data. Estimates for β_1 from the animal and human donor studies ranged from 0.20 to 0.77, so we chose 0.5 to normalize the data, i.e., $p\text{Smad}/(t\text{Smad})^{0.5}$ partly as a matter of convenience.

The normalized pSmad values were converted to percent inhibition using the vehicle (untreated) group mean, as follows:

$$\left[1 - \frac{(P/T^{0.5})}{M} \right] \cdot 100$$

where P = pSmad, T = tSmad, and M is the mean $(P/T^{0.5})$ in the vehicle lane(s).

2 Inhibition of pSmad

Percent inhibition results showed that the candidate inhibited normalized pSmad in a dose-dependent and time-dependent manner across species. Table 4 shows these results for the human donor experiment.

Table 4
Percent inhibition results for the human donor experiment.

Study	Dose, μM	% Inhibition			P-value vs Vehicle*
		Mean	SE	# of Subjects	
H1	0	-0.3	2.2	31	
	<2	5.1	1.7	31	0.385
	2.2	40.7	2.0	31	<0.001
	6.7	76.1	1.2	31	<0.001
	20	96.1	0.6	11	<0.001

* P-values from two-way ANOVA on $\text{Log}(P/T^{0.5})$ with effects for dose group and subject. Doses < 2 μM had no effect and were pooled.

Figure 4 shows the dose-response data for the human donor experiment. An IC_{50} was determined for each individual, and the mean IC_{50} was 2.9 μM , with a 95% confidence interval of 2.4 to 3.4 μM . Similar results were found in the mouse data.

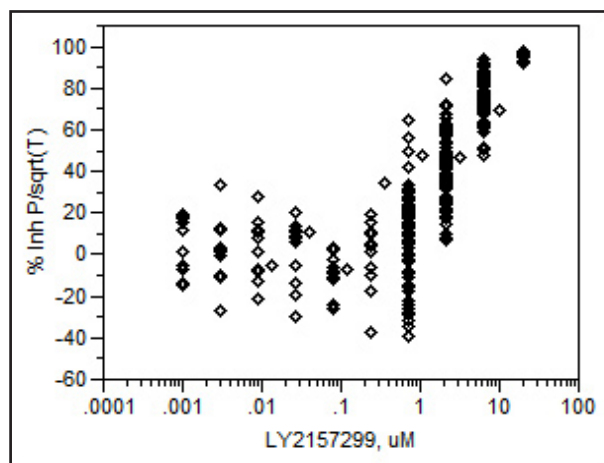


Figure 4
Human donor concentration-response data

3 Comparison of tumor and PBMC inhibition

In two rat studies, pSmad inhibition was measured in tumor tissue and in PBMC samples from the same animals. Good correlation ($r \geq 0.75$) was observed between tumor and PBMC samples in both studies. Treatment groups included an untreated control group and treated animals measured at different times post-dose (0.5, 1, 1.5, 2, 4, 8, 16, and 24 hours). The dose was 30 mg/kg in one study and 300 mg/kg in the other. The generalizability of this result could be limited since these studies used the same age and sex of animals and the same tumor xenograft. This comparison will be repeated in a clinical trial.

4 Comparison of ELISA and Western blot

For translation to the clinic, the Western blot method was changed to an ELISA (Enzyme Linked Immuno-Sorbent Assay) method. Pre-clinical experiments showed a favorable comparison between the ELISA and the Western blot. The use of this novel ELISA and its application in an ex vivo assay was evaluated in a non-drug interventional study¹². The results of this study suggest that the pSMAD ELISA performs sufficiently well to determine drug effects in patients. The application of this ELISA is now being

used for determining pharmacodynamic responses of a novel Lilly TGF- β inhibitor in patients.

Summary

Early clinical drug development in oncology requires early decisions on whether to advance a specific compound or not. Biomarkers can be used to make such early development decisions. As exemplified here for a TGF- β inhibitor, the use of a known intracellular signaling protein, such as pSMAD, can establish early activity of the inhibitor. This biomarker was used to translate potential activity of TGF- β inhibitors from non-clinical to clinical applications and thus guide the early drug development in oncology. For a TGF- β inhibitor, using pSMAD as a biomarker of activity fulfills the necessary criteria, including 1) showing modulation of pSmad both *in-vivo* and *in-vitro* samples across species, 2) normalizing data for clinical application, and 3) correlating the inhibition of pSmad in PBMC and in tumor tissue. Clinical development of this biomarker is ongoing.

Instead of normalizing the data as we have, one could use the ANCOVA directly when estimating the percentage inhibition of pSmad. One advantage of normalizing the data is to facilitate PK/PD analyses across studies using the normalized percent inhibition as the response variable. Also, we believe it may be better to fix β_1 across studies, rather than estimate it for each study, at least in the pre-clinical and early clinical phase settings where studies are relatively small. One of our goals was to use the pre-clinical data to inform the early clinical data analysis. As the clinical data accumulates, we will be able to further evaluate this approach. ■

References

- 1 Biomarkers Definition Working Group. Biomarkers and surrogate endpoints: Preferred definitions and conceptual framework. *Clinical Pharmacol. Ther.* 2001; 69:89-95
- 2 Baker, M. In biomarkers we trust? *Nature Biotechnology* 2005, Volume 23, No3, 297-304
- 3 (a) Huse, M.; Muir, R. W.; Xu, L.; Chen, Y.-G.; Kuriyan, J.; Massague, J. The TGF β Receptor Activation Process: An Inhibitor- to Substrate-Binding Switch. *Mol. Cell* 2001, 8, 671-682. (b) Moustakas, A.; Soucheinytskyi, S.; Heldin, C.-H. Smad Regulation in TGF- β Signal Transduction. *J. Cell Sci.* 2001, 114, 4359-4369. (c) Zimmerman, C. M.; Padgett, R. W. Transforming Growth factor β Signaling Mediators and Modulators. *Gene* 2000, 249, 17-30.
- 4 Kim, S. J.; Park, K.; Koeller, D.; Kim, K. Y.; Wakefield, L. M.; Sporn, M. B.; Roberts, A. B. Post-Transcriptional Regulation of the Human Transforming Growth Factor β 1 Gene. *J. Biol. Chem.* 1992, 267(19), 13702-13707.
- 5 Cordeiro, M. F. Beyond Mitomycin: TGF- β and Wound Healing. *Prog. Renal Eye Res.* 2002, 21, 75-89.
- 6 Masliah, E.; Ho, G.; Wyss-Coray, T. Functional Role of TGF β in Alzheimer's Disease Microvascular Injury: Lessons from Transgenic Mice. *Neurochem. Int.* 2001, 39, 393-400.
- 7 McCaffrey, T. A. TGF- β s and TGF- β Receptors in Atherosclerosis. *Cytokine and Growth Factor Rev.* 2000, 11, 103-114.
- 8 Derhaschnig, U.; Shehata, M.; Herkner, H.; Bur, A.; Woisetschlager, C.; Laggner, A. N.; Hirschl, M. M. Increased Levels of Transforming Growth Factor- β 1 in Essential Hypertension. *Am. J. Hypertension* 2002, 15, 207-211.
- 9 Chamberlain, J. Transforming Growth Factor-: A Promising Target for Anti-Stenosis Therapy. *Cardiovasc. Drug Rev.* 2001, 19(4), 329-344.
- 10 (a) Akhurst, R. J.; Derynk, R. TGF- β Signaling in Cancer— A Double-Edged Sword. *Trends Cell Biol.* 2001, 11(11), S44-S51. (b) Derynk, R.; Akhurst, R. J.; Balmain, A. TGF- β Signaling in Tumor Suppression and Cancer Progression. *Nature Genetics* 2001, 29, 117-129. (c) Massague, J.; Blain, S. W.; Lo, R. S. TGF- β Signaling in Growth Control, Cancer, and Heritable Disorders. *Cell* 2000, 103, 295-309. (d) de Caestecker, M. P.; Piek, E.; Roberts, A. B. Role of Transforming Growth Factor- β Signaling in Cancer. *J. Nat. Cancer Inst.* 2000, 92(17), 1388-1402.

- 11 Yingling JM, Blanchard KL, Sawyer JS. Development of TGF-beta signalling inhibitors for cancer therapy. *Nature Reviews. Drug Discovery*. 3(12):1011-22, 2004
- 12 Jose Baselga, Mace L. Rothenberg, Josep Tabernero, Joan Seoane, Thomas Daly, Jonathan Yingling, Ann

Cleverly, Brandi Berry, Susanne Kloeker, Lisa Anne Wallace, Jonathan M Yingling, Michael Lahn, Carlos Arteaga and Michael Carducci. TGF β , pSMAD and TGF β -related Markers in Patients with Advanced Metastatic Cancer. Submitted Poster to AACR 2006.).

ENAR 2007

Ann Herring

The 2007 ENAR Program Committee would like to thank the ASA Biopharmaceutical Section for its continuing support and to extend a special thanks to Amit Bhattacharyya, the section representative on the program committee.

We are very pleased to invite you to Atlanta, Georgia, March 11-14, 2007 for the ENAR Spring Meeting in conjunction with Sections of ASA and IMS! We have an exciting program planned, with strong representation from the ASA Biopharmaceutical Section, and we look forward to seeing many of you there.

We are pleased to announce that Dr. Frank Rockhold, Senior Vice President of GlaxoSmith-Kline Pharmaceuticals Research and Development, is our Presidential Invited Speaker. Dr. Rockhold has achieved considerable stature in the pharmaceutical industry while maintaining strong ties to the statistics profession and being a strong advocate of statisticians in industry. Before Dr. Rockhold's lecture, we will present the Distinguished Student Paper Awards; up to 20 awards will be presented, and details on how to apply before the November 1 deadline can be found at the ENAR website, <http://www.enar.org>. In addition, ENAR is honored to host the IMS Medallion Lecture of Dr. Robert Tibshirani. Dr. Tibshirani, Professor of Health Research and Policy and Statistics at Stanford University, has an impressive record of scholarship, teaching, and service, and he will speak on "Prediction by supervised principal components" Tuesday afternoon. In addition to our two keynote lectures,

we are looking forward to a strong group of invited sessions in emerging statistical methods and innovative applications, as well as two thought-provoking panel discussions: "Rethinking the FDA" and "Role of Biostatisticians in Policy Issues." The complete invited portion of the scientific program is available at the ENAR website, and the deadline for receiving all abstracts is November 15, 2006.

Our continuing education program is equally strong and ranges from courses at the introductory level to those addressing more advanced topics. Our short courses on Sunday include applied longitudinal analysis by Garrett Fitzmaurice of Harvard University, missing data by Joe Ibrahim of the University of North Carolina, design and analysis of non-inferiority trials by James Hung and Sue-Jane Wang of the FDA, design of targeted clinical trials by Rich Simon of NCI, latent variable modeling by Bengt Muthén of UCLA, and semiparametric theory by Butch Tsiatis of North Carolina State University. Our tutorials on Monday and Tuesday include a very hands-on WinBUGS workshop led by Brad Carlin of Minnesota, an introduction to using HapSTAT for haplotype analysis by Danyu Lin of the University of North Carolina, a foray into the land of directed acyclic graphs for causal inference by Miguel Hernán of Harvard University, and analysis of epidemic models and infectious disease data by Betz Halloran of the University of Washington. Register soon for Monday's roundtable discussions, as they cover a variety of hot topics, including a discussion

of conflict of interest led by Keith Soper, a look at the intersection between drugs and devices by Greg Campbell, surrogate endpoints by Geert Molenberghs, and power and sample size by Keith Muller.

We are also very pleased to offer the "Fostering Diversity in Biostatistics" workshop on Sunday, March 11. Please help us publicize this workshop by contacting students and faculty with ties to historically underrepresented ethnic groups so that we can exchange ideas and help them learn more about our field.

For the Tuesday evening social outing, we will dine at a nearby restaurant in a historic building in downtown Atlanta, complete with a jazz band (featuring our own Dave Kleinbaum!) for entertainment. We also urge all members to take a little extra time to enjoy Atlanta before or after the workshop. Of particular note are the new Georgia Aquarium, the world's largest aquarium, and a number of historical sites, including the Martin Luther King, Jr. National Historic Site and the home of Margaret Mitchell, author of *Gone with the Wind*. Welcome to Atlanta! ■

A New Journal! *Statistics in Biopharmaceutical Research*

Joe Heyse

In December 2005 the ASA Board of Directors approved the establishment of a new journal, *Statistics in Biopharmaceutical Research* (SBR). The idea for the new journal was originally proposed by Bradley Efron during his term as President of ASA. His intention was to provide a journal that would specifically address the growing needs of the biopharmaceutical sciences. A task force led by Karen Kafadar constructed the business case for SBR and Joe Heyse was selected to be the editor. It is expected that SBR will have strong interest among the membership of the Biopharmaceutical Section. The Biopharmaceutical Section's Executive Committee has supported the creation of SBR, having representation on the originating task force and continuing on the SBR advisory committee.

SBR will publish articles that focus on the needs of researchers and applied statisticians from academia, government, and industry. This includes papers discussing appropriate statistical methodology and information regarding the use of statistics in all phases of research, development, and practice in the pharmaceutical, biopharmaceutical, device and diagnostics industries. Articles will focus on the development of novel statistical methods, novel applications of current methods, or the innovative application of statistical principles that can be used by statistical practitioners in these disciplines.

The editorial board of SBR intends to ensure that the journal continually provides important, useful,

and timely information. To accomplish this, the board strives to attract outstanding articles by seeing that each submission receives a careful, thorough, and prompt review.

The journal was opened on July 1, 2006 to begin accepting papers through AllenTrack, a web-based manuscript submission and tracking system (<http://sbr.allentrack.net>). Publication of the first issue is targeted for late 2007. Be on the lookout for your 2007 ASA dues renewal notices that will encourage submissions to SBR and highlight the journal.

The establishment of SBR marks a tremendous commitment by the ASA to the biopharmaceutical sciences, and many people have contributed in order to get the journal to this point. Fritz Scheuren noted the importance of SBR during his president's address at the JSM in Seattle this past August and Bill Smith, ASA Executive Director, provided his strong support for SBR to the Committee on Publications. This new initiative provides an opportunity for the Biopharmaceutical Section membership to increase our visibility and support to this continually evolving area of research. Members are encouraged to submit their work to SBR, to subscribe to the journal, and to get involved by serving in other editorial capacities.

More information about SBR is available on the ASA website <http://www.amstat.org> or at the journal web site <http://sbr.allentrack.net>. Inquiries about the journal can be directed to Joe Heyse, joseph_heyse@merck.com. ■

Roundtable Sessions at the Joint Statistical Meetings

Amit Bhattacharyya

The Biopharmaceutical Section successfully sponsored 34 luncheon sessions during the JSM 2006. It's a record number of sessions! Half of the sessions had full tables with 10 participants; many (9) had 8 or more participants at the table; and a few (6) had 6 or more participants. The attendees from pharmaceutical and biotechnology companies, devices companies, contract research organizations and FDA represented the full sphere of pharmaceutical and devices research areas. Significant positive feedback was received from the chairs of the luncheon topics suggesting that the Biopharmaceutical Section continue to sponsor such sessions in the future.

Let's Hear from You!

If you have any comments or contributions, contact the Editor: Richard Caplan, phone: 302-885-5915, email: richard.caplan@astrazeneca.com; or Associate Editor: Philip Pichotta, phone: 203-882-9321, email: pichottapm@optonline.net.

We are looking for volunteers to write articles that will be of interest to our members. Some authorless topics that have been suggested include validating endpoints and working with SEALD, enhanced trial designs, recent changes in oncology research, animal studies and veterinary medicine, bioequivalence in biologics and personalized medicine. Non-technical articles related to our work are welcome. If you have been working in an area and would like to suggest a topic or volunteer to write, please send us an email.

The *Biopharmaceutical Report* is a publication of the Biopharmaceutical Section of the American Statistical Association.