Table of Contents

An AACR Conference on
Translational Cancer Medicine 2010 (Europe)
March 21-24, 2010 • RAI Exhibition and Convention Centre • Amsterdam, The Netherlands

Conference Chairpersons:
Alexander M.M. Eggermont
Erasmus Medical Center,
Rotterdam, The Netherlands
Susan E. Bates,
National Cancer Institute,
Bethesda, MD, USA

Welcome .................................................................................................................. 3
Maps ....................................................................................................................... 4
Committees ............................................................................................................. 5
About the AACC ..................................................................................................... 6
Awards and Educational Grants ........................................................................... 7
General Information ............................................................................................ 8
Scientific Program ................................................................................................ 9
Supporters ............................................................................................................. 10
Conference Program and Schedule ................................................................. 11

Sunday, March 21 .................................................................................................. 11
   Educational Session 1: Omics and Bioinformatics ........................................... 11
   Educational Session 2: Translational and Clinical Trial Design ..................... 11
   Educational Session 3: GWAS vs. Systems Biology ........................................ 11
   Educational Session 4: Functional Imaging:
      Getting Beyond FDG-PET ............................................................................... 11
Keynote Session .................................................................................................. 11

About the Cover:
1. CNS-1 rat glioblastoma cells were infected with high-capacity adenoviral vectors encoding β-galactosidase under the control of a third-generation Tet-On system (image shows expression off). Reprinted from figure 1A: Curtin, JF, et al., Mol Cancer Ther 2008;7(3):439-48.
3. All-to-all Tanimoto scores for true positive and true negative compounds for CNS tumor panel. Reprinted from figure 5: Covell, DG, et al., Mol Cancer Ther 2007 6(8):2261-70.
7. CNS-1 rat glioblastoma cells were infected with high-capacity adenoviral vectors encoding β-galactosidase under the control of a third-generation Tet-On system (image shows expression on). Reprinted from figure 1A: Curtin, JF, et al., Mol Cancer Ther 2008;7(3):439-48.
# Table of Contents

**Monday, March 22**
- Plenary Session 1: Translational Medicine in Breast Cancer Research ......................................................... 12
- Poster Session A .................................................................................................................................................. 12
- Concurrent Session 1: Mutations in Malignancy .............................................................................................. 12
- Concurrent Session 2: Immunotherapy ............................................................................................................. 12
- Plenary Session 2: Translational Medicine in Lung Cancer Research ............................................................. 12

**Tuesday, March 23**
- Plenary Session 3: Translational Medicine in Multiple Myeloma ................................................................. 13
- Poster Session B ................................................................................................................................................... 13
- Concurrent Session 3: Circulating Tumor Cells and Stem Cells ...................................................................... 13
- Concurrent Session 4: Pharmacogenomics, Drug Resistance, and Toxicity ..................................................... 13
- Plenary Session 4: Immunotherapy: Vaccines .................................................................................................. 13

**Wednesday, March 24**
- Plenary Session 5: Targets Across Tumor Types ............................................................................................ 14
- Plenary Session 6: Resistance to Targeted Therapies ...................................................................................... 14
- Plenary Session 7: Epigenetics .......................................................................................................................... 14

**Proceedings**
- Poster Session A .................................................................................................................................................. 23
- Poster Session B .................................................................................................................................................. 36
- Invited Abstracts .................................................................................................................................................. 50

**Abstract Author Index** .................................................................................................................................. 60
Dear Colleagues,

On behalf of the American Association for Cancer Research, we would like to welcome you to Amsterdam, The Netherlands, for the fourth conference in the AACR’s Translational Cancer Medicine conference series. Conferences in this series bring together and foster discussion and collaboration between clinicians and basic scientists from academia, industry, and government from all over the world. Our goal is to strengthen translational cancer medicine and to reduce the barriers to progress in oncology. Highlighting this program will be a keynote address by René Bernards titled “Finding mechanisms and biomarkers of drug resistance in cancer.”

We would like to thank the Scientific Program and Review committees for their help developing such an outstanding program. We are grateful to Underwriting Supporter Amgen, Inc. and Major Supporter Bristol-Myers Squibb Company for their support of this educational activity, and to AstraZeneca; Aflac, Inc.; and the Avon Foundation for their support of the Scholar-in-Training awards and grants.

Best wishes for a fantastic meeting,

Alexander M.M. Eggermont  
Susan E. Bates
Committees

**Conference Chairpersons:**

Alexander M.M. Eggermont, Erasmus Medical Center, Rotterdam, The Netherlands  
Susan E. Bates, National Cancer Institute, Bethesda, MD, USA

**Scientific Program Committee:**

José Baselga, Vall d’Hebron University Hospital, Barcelona, Spain  
Kapil N. Bhalla, Medical College of Georgia, Augusta, GA, USA  
Anne-Lise Børresen-Dale, Norwegian Radium Hospital, Oslo, Norway  
Stephen J. Chanock, National Cancer Institute, Bethesda, MD, USA  
Johann S. de Bono, Institute of Cancer Research, Sutton, United Kingdom  
E. G. Elisabeth de Vries, University Medical Center Groningen, Groningen, The Netherlands  
John A. Foekens, Erasmus Medical Center, Rotterdam, The Netherlands  
Nadia Harbeck, University of Cologne, Cologne, Germany  
Toshihisa Ishikawa, RIKEN Yokohama Institute, Yokohama, Japan  
J. Jack Lee, UT M. D. Anderson Cancer Center, Houston, TX, USA  
Jennifer A. Low, Genentech, Inc., South San Francisco, CA, USA  
Richard M. Marais, Institute of Cancer Research, London, United Kingdom  
Julia A. Newton Bishop, University of Leeds, Leeds, United Kingdom

Pier Giuseppe Pelicci, European Institute of Oncology, Milan, Italy  
Marco A. Pierotti, National Cancer Institute, Milan, Italy  
Mark J. Ratain, University of Chicago, Chicago, IL, USA  
Eddie Reed, University of South Alabama, Mobile, AL, USA  
Eric H. Rubin, Merck Research Laboratories, North Wales, PA, USA  
Howard I. Scher, Memorial Sloan-Kettering Cancer Center, New York, NY, USA  
Jean-Charles Soria, Institut Gustave-Roussy, Villejuif, France  
Laura J. van’t Veer, UCSF Helen Diller Comprehensive Cancer Center, San Francisco, CA, USA  
Otmar D. Wiestler, German Cancer Research Center, Heidelberg, Germany  
John E.L. Wong, National University of Singapore, Singapore  
John J. Wright, National Cancer Institute, Rockville, MD, USA

**Scientific Review Committee:**

Alexander M.M. Eggermont, Erasmus Medical Center, Rotterdam, The Netherlands  
Susan E. Bates, National Cancer Institute, Bethesda, MD, USA  
Tito Fojo, NCI-DHHS, Bethesda, MD, USA  
Richard M. Marais, Institute of Cancer Research, London, United Kingdom

Translational Cancer Medicine 2010 (Europe) • March 21-24, 2010 • Amsterdam, The Netherlands
The American Association for Cancer Research (AACR) is a professionalsociety of more than 30,000 basic, translational and clinical researchers; health care professionals; and cancer survivors and advocates in the United States and nearly 90 other countries. Founded in 1907, the AACR has as its mission to accelerate the prevention and cure of cancer through research, education, communication, collaboration, and advocacy. The AACR publishes six major peer-reviewed journals: Cancer Research; Clinical Cancer Research; Molecular Cancer Therapeutics; Molecular Cancer Research; Cancer Epidemiology, Biomarkers & Prevention; and Cancer Prevention Research.

The AACR also publishes CR, a magazine for cancer survivors, patient advocates, their families, physicians, and scientists. CR provides a forum for sharing essential, evidence-based information and perspectives on progress in cancer research, survivorship, and advocacy.

The AACR Annual Meeting attracts more than 16,000 participants who share the latest discoveries and developments in the field. Special conferences throughout the year present novel data across a wide variety of topics in cancer research, treatment, and patient care.

To foster the training and development of the next generation of cancer researchers, the AACR offers reduced rates for memberships and journal subscriptions to young investigators, a job web site, and special educational programs designed for early-career scientists. The AACR also sponsors career development awards for this group, to ease the transition to faculty status, and funds travel awards for attendance at AACR meetings. Financial assistance from corporate and non-profit partners enables the AACR to offer grants to post-doctoral and clinical fellows working in basic, translational, clinical, and prevention research.

For more information on AACR’s mission and activities, please visit the AACR’s website, www.aacr.org.
Scholar-in-Training Awards and Grants

Fifteen presenters of abstracts have been selected by the Scientific Review Committee to receive awards or grants to attend this conference. All graduate and medical students, postdoctoral fellows, and physicians-in-training were eligible for consideration. The names of the Scholar-in-Training Awardees and Grantees, their affiliations, and the poster numbers of their abstracts are provided below. AACR sincerely thanks Aflac, Inc., AstraZeneca, and the Avon Foundation for their generous support of these awards and grants.

AACR-Aflac, Inc. Scholar-in-Training Awards

David Barron, Baylor College of Medicine, Houston, TX, USA, B23
Juliann Chmielecki, Weill Cornell Graduate School of Medical Sciences, New York, NY, USA, A18
John S.W. Low, Cancer Science Institute of Singapore, National University of Singapore, Singapore, Singapore, B33
Nicholas F. Marko, Cleveland Clinic, Cleveland, OH, USA, B8
Michele L. Martin, BC Cancer Agency, Vancouver, BC, Canada, B12
Rebecca C. Obeng, University of Virginia, Charlottesville, VA, USA, B14
April Rose, McGill University, Montreal, QC, Canada, A8
Nathan West, BC Cancer Agency, Victoria, BC, Canada, B13
Julie Ann Woolworth, Medical University of South Carolina, Charleston, SC, USA, B26

AACR-AstraZeneca International Scholar-in-Training Awards

Hadeel Khallouf, University of Heidelberg, Heidelberg, Germany, B15
Raya Leibowitz-Amit, The Chaim Sheba Medical Center, Tel-Hashomer, Israel, A17
Fayaz Malik, Indian Institute of Integrative Medicine, Jammu, India, A13
Sven Rottenberg, The Netherlands Cancer Institute, Amsterdam, The Netherlands, A14
Katharina Tomek, Medical University Vienna, Vienna, Austria, A6

Avon Foundation Scholar-in-Training Grant

Chinmoy K. Bose, Netaji Subhash Chandra Bose Cancer Research Institute, Kolkata, India, A19
Location of the Session Rooms

The conference is being held at the Amsterdam RAI Exhibition and Convention Centre.

Entrance E is the dedicated entrance for this conference.

Amsterdam RAI Exhibition and Convention Centre
Europaplein 22
NL 1078 GZ Amsterdam
Phone: +31 (0)20 549 1212

Plenary Sessions: Forum
Concurrent Sessions: E102
Poster Sessions: Forum Lounge
Catering: Forum Lounge and Ruby Lounge

Coffee Breaks
The coffee breaks will be held in the Forum Lounge (ground level):
- Sunday, March 21 17:15-18:00
- Monday, March 22 10:30-11:30 and 16:00-16:15
- Tuesday, March 23 10:30-11:30 and 15:30-16:00
- Wednesday, March 24 10:30-10:45

Lunches
Complimentary lunch is served in the Ruby Lounge (Level 1):
- Monday, March 22 12:30-14:00
- Tuesday, March 23 12:30-13:30
- Wednesday, March 24 12:45-13:45

No Smoking Regulations
In accordance with the Resolution adopted at the 1968 Annual Meeting of the American Association for Cancer Research, registrants must refrain from smoking in all meeting rooms. This regulation applies to all session rooms, including the exhibit and poster area. Additionally, smoking is not permitted in the Amsterdam RAI Exhibition and Convention Centre.

Cell Phones/Beepers
As a courtesy to your colleagues, please turn off your cell phone or beeper, or set it on silent mode before you enter any room in which a lecture session is taking place.

Certificates of Attendance
Certificates of attendance are available at the conference registration desk as of Wednesday, March 24, 08:00.

Assistance for Physically Challenged Registrants
Registrants with special requirements for transportation should notify a member of the AACR staff at the registration desk upon arrival at the conference.

Conference Registration
Conference registration will be held in the RAI Forum Lounge. Registration will be open on the following schedule:

- Sunday, March 21 08:00-20:00
- Monday, March 22 07:30-18:30
- Tuesday, March 23 07:30-18:30
- Wednesday, March 24 07:30-15:00

Internet Zone
There will be an Internet Zone available for attendees to check their e-mail while away from the office. The Internet Zone will be located in the Forum Lounge (ground level).

Reception and Meals
Opening Reception
The opening reception will be held Sunday, March 21 from 19:00-21:00 in the Ruby Lounge. All registrants are invited to attend. There will be hors d’oeuvres/finger food and beverages served. Conference badges are required.
Scientific Program

Lecture Sessions
The program includes seven major Plenary Sessions that are designed to cover major topics in translational cancer medicine. These sessions will be supplemented with four educational sessions at the beginning of the conference, one keynote session, and four concurrent sessions. Please refer to the conference program on pages 11-14 for a complete listing of all sessions.

Poster Sessions
Abstracts will be presented at the two poster sessions on March 22 and 23. Poster sessions will be held in the Forum Lounge according to the following schedule:

Poster Session A  Monday, March 22  10:30-12:30
Poster Session B  Tuesday, March 23  10:30-12:30

All presenters must stand by their posters for at least 90 minutes of the two-hour poster session. Presenters can set up and take down their posters according to the following schedule:

Poster Session A (March 22, 10:30-12:30), set up starting at 17:30 on March 21, take down by 16:00 on March 22;

Poster Session B (March 23, 10:30-12:30), set up starting at 16:30 on March 22, take down by 18:00 on March 23.
Supporters

Underwriting Supporter

AMGEN

Major Supporter

Bristol-Myers Squibb
Oncology Division

Supporters for Scholar-in-Training Awards and Grants

Aflac

AstraZeneca

AVON Foundation
Conference Program and Schedule

Sunday, March 21, 2010

13:00-15:00 Educational Session 1: Omics and Bioinformatics E102
Chairperson: Olli-P. Kallioniemi, Finland Institute for Molecular Medicine, Helsinki, Finland

From canceromics research to personalized cancer therapies
Olli-P. Kallioniemi, Finland Institute for Molecular Medicine, Helsinki, Finland

The role of informatics in translational research: The interplay of epidemiology, clinical studies, and discovery research*
Jacob Koehler, Eli Lilly and Company, Indianapolis, IN, USA

Title to be announced
John N. Weinstein, UT M. D. Anderson Cancer Center, Houston, TX, USA

13:00-15:00 Educational Session 2: Translational and Clinical Trial Design Forum
Chairperson: Eric H. Rubin, Merck Research Laboratories, North Wales, PA, USA

Approaches to solving the combinations problem in oncology therapeutics
Eric H. Rubin, Merck Research Laboratories, North Wales, PA, USA

Translational genomics in clinical trials
Carlos M. Caldas, Cancer Research UK, Cambridge, United Kingdom

Title to be announced
Laura J. van’t Vee, UCSF Helen Diller Family Comprehensive Cancer Center, San Francisco, CA, USA

15:15-17:15 Educational Session 3: GWAS vs. Systems Biology Forum
Chairperson: Stephen J. Chanock, National Cancer Institute, Bethesda, MD, USA

Genome-wide association studies in cancer: Insights in cancer etiology*
Stephen J. Chanock, National Cancer Institute, Bethesda, MD, USA

Understanding melanoma using GWAS and systems biology*
Julia A. Newton Bishop, University of Leeds, Leeds, United Kingdom

Etiological clues from breast cancer GWAS*
Montserrat Garcia-Closas, NC1-DCEG, Rockville, MD, USA

15:15-17:15 Educational Session 4: Functional Imaging: Getting Beyond FDG-PET E102
Chairperson: E. G. Elisabeth de Vries, University Center, Groningen, The Netherlands

Functional imaging: Beyond FDG*
Patricia M. Price, Christie Hospital NHS Trust, Manchester, United Kingdom

Functional imaging: Getting beyond FDG-PET*
E. G. Elisabeth de Vries, University Medical Center Groningen, Groningen, The Netherlands

PET tracer for therapy monitoring*
Hans-Jürgen Wester, Technische Universität München, Munich, Germany

17:15-18:00 Coffee Break Forum Lounge

18:00-19:00 Keynote Session Forum
Chairpersons: Alexander M. M. Eggermont, Erasmus Medical Center, Rotterdam, The Netherlands and Susan E. Bates, National Cancer Institute, Bethesda, MD, USA

Finding mechanisms and biomarkers of drug resistance in cancer*
René Bernards, Netherlands Cancer Institute, Amsterdam, The Netherlands

19:00-21:00 Opening Reception Ruby Lounge

*An extended abstract for this presentation is available in the Invited Abstracts section of the Proceedings.
Monday, March 22, 2010

08:30-10:30  Plenary Session 1: Translational Medicine in Breast Cancer Research Forum

Chairperson: Nadia Harbeck, University of Cologne, Cologne, Germany

Targeting PI3K in breast cancer
José Baselga, Vall d’Hebron University Hospital, Barcelona, Spain

Genomic architecture characterizes tumor progression paths and fate in breast cancer patients*
Anne-Lise Børresen-Dale, Norwegian Radium Hospital, Oslo, Norway

Amplifying the apoptotic actions of estrogen to treat metastatic breast cancer
V. Craig Jordan, Lombardi Comprehensive Cancer Center, Washington, DC, USA

10:30-11:30  Coffee Break

10:30-12:30  Poster Session A

12:30-14:00  Lunch/Networking Break

14:00-16:00  Concurrent Session 1: Mutations in Malignancy Forum

Chairperson: Marco A. Pierotti, National Cancer Institute, Milan, Italy

Target mutation: The dark side of the targeted therapies*
Marco A. Pierotti, National Cancer Institute, Milan, Italy

Genetic alterations in melanoma: Implications for disease classification and therapy stratification
Boris C. Bastian, UCSF Helen Diller Family Comprehensive Cancer Center, San Francisco, CA, USA

Mutations and expression profile to guide treatment in sarcomas and GIST*
Jean-Yves Blay, INSERM U-453, Lyon, France

14:00-16:00  Concurrent Session 2: Immunotherapy

Chairperson: Cornelis J.M. Melief, University Hospital Leiden, Leiden, The Netherlands

Personalized chemotherapy of cancer based on immune parameters*
Laurence Zitvogel, Institute Gustave-Roussy, Villejuif, France

Adoptive T cell transfer: Autografting cultured, specific T cells to treat cancer
James Chung-Yin Yang, National Cancer Institute, Bethesda, MD, USA

Development of therapeutic cancer vaccine and construction of clinical research network in Japan*
Yusuke Nakamura, University of Tokyo Human Genome Center, Tokyo, Japan

16:00-16:15  Coffee Break

16:15-18:15  Plenary Session 2: Translational Medicine in Lung Cancer Research Forum

Chairperson: Giuseppe Giaccone, National Cancer Institute, Bethesda, MD, USA

The impact of genomic changes on the treatment of lung cancer*
Bruce E. Johnson, Dana-Farber Cancer Institute, Boston, MA, USA

The genomic landscape in lung cancer*
Rafael Rosell, Catalan Institute of Oncology, Hospital Germans Trias I Pujol, Badalona, Spain

Small cell lung cancer: A forgotten disease?
Giuseppe Giaccone, National Cancer Institute, Bethesda, MD, USA

*An extended abstract for this presentation is available in the Invited Abstracts section of the Proceedings.
**Tuesday, March 23, 2010**

<table>
<thead>
<tr>
<th>Time</th>
<th>Session/Activity</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>08:30-10:30</td>
<td>Plenary Session 3: Translational Medicine in Multiple Myeloma Forum</td>
<td>Chairperson: Jesús F. San Miguel, University of Salamanca, Salamanca, Spain. Biology of myeloma: Basis for novel drugs* Jesús F. San Miguel, University of Salamanca, Salamanca, Spain. Translating multiple myeloma stem cells* William H. Matsui, Johns Hopkins University School of Medicine, Baltimore, MD, USA. Targeting the ubiquitin-proteasome pathway in myeloma therapy Robert Z. Orloffski, UT M. D. Anderson Cancer Center, Houston, TX, USA.</td>
</tr>
<tr>
<td>10:30-11:30</td>
<td>Coffee Break</td>
<td>Forum Lounge</td>
</tr>
<tr>
<td>10:30-12:30</td>
<td>Poster Session B</td>
<td>Forum Lounge</td>
</tr>
<tr>
<td>12:30-13:30</td>
<td>Lunch</td>
<td>Ruby Lounge</td>
</tr>
<tr>
<td>13:30-15:30</td>
<td>Concurrent Session 3: Circulating Tumor Cells and Stem Cells Forum</td>
<td>Chairperson: Howard I. Scher, Memorial Sloan-Kettering Cancer Center, New York, NY, USA. Detection, clinical relevance, and molecular characteristics of circulating tumor cells* Klaus Pantel, University Medical Center Hamburg-Eppendorf, Hamburg, Germany. Enumeration and characterization of CTCs* Stefan Sleijfer, Erasmus Medical Center, Rotterdam, The Netherlands. Molecular analysis of single disseminated tumor cells Christoph A. Klein, University of Regensburg, Regensburg, Germany.</td>
</tr>
<tr>
<td>15:30-16:00</td>
<td>Coffee Break</td>
<td>Forum Lounge</td>
</tr>
<tr>
<td>16:00-18:30</td>
<td>Plenary Session 4: Immunotherapy: Vaccines Forum</td>
<td>Chairperson: Laurence Zitvogel, Institute Gustave-Roussy, Villejuif, France. Immunostimulation versus immunosuppression: The woes of cancer vaccine development Alexander M.M. Eggermont, Erasmus Medical Center, Rotterdam, The Netherlands. Therapeutic vaccines for prostate cancer James L. Gulley, National Cancer Institute, Bethesda, MD, USA.</td>
</tr>
</tbody>
</table>

*An extended abstract for this presentation is available in the Invited Abstracts section of the Proceedings.*

**Translation Cancer Medicine 2010 (Europe)** • March 21-24, 2010 • Amsterdam, The Netherlands
Augmenting the immune response to prostate cancer with CTLA-4 blockade
Eric J. Small, UCSF Helen Diller Family Comprehensive Cancer Center, San Francisco, CA, USA

A new era for dendritic cell vaccines
Gerold Schuler, University Hospital of Erlangen, Erlangen, Germany

Immunotherapy of established lesions caused by high-risk HPV*
Cornelis J.M. Melief, University Hospital Leiden, Leiden, The Netherlands

Wednesday, March 24, 2010

08:30-10:30 Plenary Session 5: Targets Across Tumor Types
Forum

Chairperson: Keith T. Flaherty, Massachusetts General Hospital, Boston, MA, USA

Targeting the nexus of heat shock and metabolic stress responses in cancer*
Kapil N. Bhalla, Medical College of Georgia, Augusta, GA, USA

BRAF mutant melanoma as the proving ground for the MAP kinase pathway as a therapeutic target
Keith T. Flaherty, Massachusetts General Hospital, Boston, MA, USA

Hedgehog pathway inhibitors in cancer
Josina C. Reddy, Genentech, Inc., South San Francisco, CA, USA

Targeting DNA repair mechanisms
E. Ruth Plummer, Northern Centre for Cancer Treatment, Newcastle upon Tyne, United Kingdom

10:30-10:45 Coffee Break
Forum Lounge

10:45-12:45 Plenary Session 6: Resistance to Targeted Therapies
Forum

Chairperson: Tito Fojo, NCI-DHHS, Bethesda, MD, USA

Resistance to targeted therapies in a realistic mouse breast cancer model*
Piet Borst, Netherlands Cancer Institute, Amsterdam, The Netherlands

Resistance to VEGF-targeted therapies
Napoleon Ferrara, Genentech, Inc., South San Francisco, CA, USA

Antibody-initiated cancer immunotherapy*
Louis M. Weiner, Georgetown Lombardi Comprehensive Cancer Center, Washington, DC, USA

Title to be announced
Howard I. Scher, Memorial Sloan-Kettering Cancer Center, New York, NY, USA

12:45-14:00 Lunch
Ruby Lounge

14:00-15:30 Plenary Session 7: Epigenetics
Forum

Chairperson: Susan E. Bates, National Cancer Institute, Bethesda, MD, USA

Cancer epigenetics: From DNA methylation to microRNAs
Manel Esteller, Hospital Duran i Reynals, Barcelona, Spain

Targeting histone methyl transferase and demethylases in cancer
Kristian Helin, University of Copenhagen, Copenhagen, Denmark

HDAC inhibitor activity in lymphomas and resistance in solid tumors: Overcoming the impasse
Susan E. Bates, National Cancer Institute, Bethesda, MD, USA

*An extended abstract for this presentation is available in the Invited Abstracts section of the Proceedings.