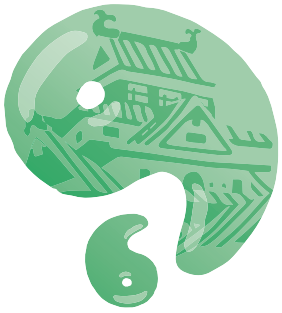


Scientific Program

The 10th International Congress on Cutaneous Adverse Drug Reactions

iSCAR 2018

SCAR1-1

Epidemiology of severe cutaneous adverse reactions（SCAR）

Maja Mockenhaupt

Medical Center and Medical Faculty-University of Freiburg, Germany

Stevens-Johnson syndrome（SJS）/toxic epidermal necrolysis（TEN）are severe, life-threatening muco-cutaneous reactions, often caused by drugs, but sometimes by infections. It is widely accepted that SJS/TEN are a single disease entity of different severity that occurs in all age groups and ethnicities. SJS/TEN has to be separated from erythema multiforme majus（EMM）but also from generalized bullous fixed drug eruption（GBFDE）, due to different clinical pattern, demographic data and causes. Drug reaction with eosinophilia and systemic symptoms（DRESS）and acute generalized exanthematous pustulosis（AGEP）are non-blistering types of SCAR. Several epidemiologic studies have investigated frequency and risk factors of these conditions.

Biography

January 1990	Begin of research fellowship and residency in dermatology at the Dept. of Dermatology, Medical Center-University of Freiburg, Germany, establishing the population-based registry on severe skin reactions in Germany（dZh）; start-up grant by BMFT（no. 0701 564/4）; 1996-2000 grant by BfArM（no. GS 1-68502-200）and 2001-2002 grant by BfArM（no. Z121.01-68502-208）
June 1996	Board-exam after residency in dermatology（Fachärztin für Haut- und Geschlechtskrankheiten）
January 2000	Appointment as senior physician（Oberärztin）at the Dept. of Dermatology, Medical Center-University of Freiburg, Germany with daily responsibilities in in- and outpatient services
1992-1996	Participation in the International Case-Control Study of Severe Cutaneous Adverse Reactions（SCAR-study）; grant by EC-BIOMED（no. BMH1-CT92-1320）
1997-2001	Organization of the European Ongoing Case-Control Surveillance of Severe Cutaneous Adverse Reactions（EuroSCAR-study）
Since Sept. 2002	Responsible coordinator of the European/International Registry of SCAR to Drugs and Collection of Biological Samples（RegiSCAR-study）; grant by EC（no. QLRT-2002-01738）
2011-2014	Systematic Review of treatment for SJS/TEN ; grant by BMBF（no. 01KG1018）
Since 1996	Reviewer for various international medical journals
Since 2010	Member of the editorial board of Acta Dermatovenereologica, section editor of drug eruptions for UpToDate Dermatology and member of the editorial board of Dermatologica Sinica

Current position：
Professor of the Medical Faculty of the Albert-Ludwigs-University, Freiburg（since Oct. 2011）
Managing senior physician of the Dept of Dermatology, Medical Center-University of Freiburg
Head of the German Registry of severe skin reactions and coordinator of the multinational RegiSCAR-project

SCAR1-2

What's New In SCAR

Elizabeth J. Phillips

Professor of Medicine and Pharmacology,
John A. Oates Chair in Clinical Research,
Vanderbilt University Medical Center, USA

Over the last 15 years there has been significant progress in our understanding of the pharmacogenetic risk for severe cutaneous adverse drug reactions and this has led to many new discoveries and widespread and successful pre-treatment screening strategies for HLA-B*15：02 and carbamazepine. The latest development in SCAR research will be discussed and models are proposed for the immunopathogenesis for SCAR that will help us understand why not all patients carrying an HLA risk allele develop disease.

Biography

Dr.Phillips a physician scientist clinically trained in Infectious diseases and clinical pharmacology who has established new clinical and research programs in drug hypersensitivity, pharmacogenomics and personalized immunology across different healthcare systems. Her laboratory is studying the immunopathogenesis of drug hypersensitivity reactions and the science of the interaction between drugs and HLA molecules and translating this into high throughput pre-clinical screening programs to inform drug safety and design. Her lab is also developing ex vivo diagnostic methods for severe immunologically mediated adverse drug reactions. Her clinical program is paired with the research program and is focused on using reconciliation and testing strategies to improve the precision of the drug allergy label, promoting the safety of drugs and reducing the allergy over-labeling that particularly occurs with antibiotics.

Amongst her greatest translational accomplishments between 2002-2008 she led the development of the HLA-B*57：01 genetic predictor for abacavir hypersensitivity from its discovery through the execution of the first clinical trial that was studied in a randomized and double blinded fashion to test the utility of a specific genetic marker, HLA-B*57：01 to predict and prevent a specific toxicitiy, abacavir hypersensitivity. Important work accomplished since the implementation of HLA-B*57：01 testing has been in elucidating the specific immunopathogenesis of abacavir hypersensitivity and other immunology-mediated drug hypersensitivity syndromes. She maintains an active research program and research institute in Perth Western Australia at the Institute for Immunology and Infectious Diseases which is funded by the National Health and Research Council of Australia.

SCAR1-3

Knowledge of genetic screening for SCAR among Canadian specialists.

R. Dodiuk-Gad, F. Chan, Neil H. Shear

University of Toronto, Canada

Over 2,000 Toronto-based, university-affiliated physicians were sent an on-line survey. Toronto has a large Asian population. Our inquiry into awareness of genetic screening for SCAR also taught core knowledge. 15% of surveys were returned. Narrative replies showed 1) some awareness of SCAR (mostly allopurinol) and 2) concern of being unaware of screening. Several will start screening and add it to teaching curriculum. Overall awareness was low, but high interest was promising. Policies are needed from health authorities.

Biography

Professor Shear is Head of Dermatology at Sunnybrook Health Sciences Centre at the University of Toronto. His primary academic research is in Drug Safety, including basic mechanisms that lead to increased risk for drug-induced harm. His practice is in complex advanced medical dermatology. Diseases of focus are atopic dermatitis, psoriasis, auto-immune blistering disease, drug-induced diseases, hidradenitis suppurativa, cutaneous lymphomas and auto-immune skin disease.

His training is in Engineering Science (University of Toronto), Medicine (McMaster), Internal Medicine (FRCPC, FACP), Dermatology (FRCPC, FAAD) and Clinical Pharmacology (Hospital for Sick Children, Toronto).

Past positions include President of the Canadian Society of Clinical Pharmacology, President of the Canadian Professors of Dermatology, President of the Canadian Dermatology Foundation and Head of Dermatology at University of Toronto. He has been an honoured visiting professor over 50 times, made an honorary member of the Société Française de Dermatologie (2017) and the Scottish Dermatological Society, recipient of the Lifetime Achievement Award of the Ontario Medical Association, and many teaching awards. Dr. Shear has been an author of over 60 text book chapters and over 350 peer-reviewed publications. And he has had the pleasure of mentoring 40 postgraduate fellows from Canada and abroad；as well as a large number of dermatologists and clinical pharmacologists in Canada.

SCAR2-1

Clinical experience on ELISpot assay for drug allergy management

Jettanong Klaewsongkram

Chulalongkorn University, Thailand

Drug allergy confirmation is a difficult task, particularly in severe cutaneous adverse reactions. The measurement of drug-specific interferon-gamma（IFN-γ）releasing cells by using enzyme-linked Immunospot（ELISpot）assay has been introduced to identify the culprit drugs in problematic cases. According to the 5 years' data in King Chulalongkorn Memorial Hospital, drugs with positive IFN-gamma ELISpot are 25 times more likely to be the culprit drugs compared to those with negative result. A significant correlation between ALDEN scores and drug-specific IFN-γ release cells in Stevens-Johnson syndrome was observed.

Biography

Institution：
Skin and Allergy Research Unit, Division of Allergy and Clinical Immunology, Department of Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand

Education：
MD. Faculty of Medicine, Chulalongkorn University
Thai Board of Internal Medicine ＆ Allergy and Clinical Immunology, Chulalongkorn University

Position：
Associate professor, Division of Allergy and Clinical Immunology, Department of Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand

Research interest：
In vitro tests for drug allergy diagnosis

SCAR2-2

SCAR pharmacogenomics in pediatric patients in Canada

Bruce C. Carleton [1,2,3]

[1] Professor（Pediatrics） & Co-Chair, Division of Translational Therapeutics, Faculty of Medicine, University of British Columbia, Canada
[2] Director, Pharmaceutical Outcomes Programme, BC Children's Hospital, Canada
[3] Senior Clinician Scientist, Child & Family Research Institute, Canada

The Canadian Pharmacogenomics Network for Drug Safety（CPNDS）consists of 26 academic healthcare centres in Canada, recruiting patients via active surveillance. The CPNDS has used this methodology to study the pharmacogenomics of severe cutaneous adverse drug reactions（cADRs）and were the first to confirm the role of *HLA* markers for carbamazepine related skin reactions in children. In collaboration with the EpiPGX Consortium, we have assembled over 80 European-descent severe cADRs cases from anticonvulsants and are currently performing a genome-wide assessment of these patients employing both genotyping arrays and exome sequencing.

Biography

Positions and Employment

1991-1993	*Clinical Pharmacotherapy Specialist*, University Hospital（Shaughnessy Site）, University of British Columbia, Vancouver, British Columbia
1991-1994	*Assistant Professor*, University of British Columbia, Vancouver, British Columbia
1991-present	*Clinical Pharmacotherapy Specialist*, BC Children's Hospital, Vancouver, British Columbia
1994-1999	*Assistant Professor*, Tenure-Track, University of British Columbia, Vancouver, British Columbia
1994-present	*Director*, Pharmaceutical Outcomes and Policy Innovations Programme, BC Children's Hospital, Vancouver, British Columbia
1996-2002	*Associate Member*, Centre for Evaluation Sciences, British Columbia Research Institute for Child and Family Health Columbia, Vancouver, British Columbia
1999-2008	*Associate Professor*, Tenured, Faculty of Pharmaceutical Sciences, University of British Columbia,
2001-2004	*Chair*, Division of Clinical Pharmacy, Vancouver, British Columbia
2002-2005	*Clinician Scientist*, Centre for Healthcare Innovation & Improvement, Child and Family Research Institute, Vancouver, British Columbia
2003-2008	*Adjunct Associate Professor*, School of Health Information Science, University of Victoria
2004-present	*Associate Member*, Centre for Health Services and Policy Research, Vancouver, British Columbia
2005-2006	*Clinical Lead*, British Columbia Ministry of Health/PharmaCare, Vancouver, British Columbia
2005-2008	*Associate Member*, Department of Paediatrics, Faculty of Medicine, University of British Columbia
2005-present	*Senior Clinician Scientist*, Child & Family Research Institute, Vancouver, British Columbia
2008-2009	*Professor*, Pharmaceutical Sciences, University of British Columbia, Vancouver, British Columbia
2008-present	*Adjunct Professor*, School of Health Information Science, University of Victoria, British Columbia
2008-present	*Professor*, Faculty of Medicine（Paediatrics）, University of British Columbia, Vancouver, British Columbia
2009-present	*Associate Member*, Pharmaceutical Sciences, University of British Columbia, Vancouver, British Columbia
2010-present	*Affiliated Investigator*, Vancouver Coastal Health Research Institute, Vancouver, British Columbia
2010-present	*Co-chair*, Division of Translational Therapeutics, Faculty of Medicine, University of British Columbia
2011-present	*Associate Member*, School of Population & Public Health, Faculty of Medicine, University of British Columbia
2011-present	*Director*, Therapeutic Evaluation Unit, British Columbia Provincial Health Services Authority
2012-present	*Associate Member*, Department of Medical Genetics, Faculty of Medicine, University of British Columbia

SCAR2-3

Genetic Predisposition and Pathology of Stevens-Johnson Syndrome with Severe Ocular Complications

Mayumi Ueta

Department of Frontier Medical Science and Technology for Ophthalmology, Kyoto Prefectural University of Medicine, Kyoto, Japan

Stevens-Johnson syndrome（SJS）is an acute inflammatory vesiculobullous reaction of the skin and mucosa, such as the ocular surface, oral cavity, and genitals. In patients with extensive skin detachment and a poor prognosis, the condition is called toxic epidermal necrolysis（TEN）. Severe ocular complications（SOC）appear in not all, but some of SJS/TEN patients who diagnosed by dermatologists. Moreover, cold medicines including multi-ingredient cold medications and NSAIDs were the main causative drugs for especially SJS/TEN with SOC in all SJS and TEN. In this symposium, I will talk about genetic predisposition and pathology of cold medicine related SJS/TEN with SOC.

Biography

1990	M.D., Graduated from Kochi Medical School
1999	Graduate student, Kyoto Prefectural University of Medicine
2000	Reseach fellow, Research Institute for Microbial Diseases, Osaka University
2003	Ph.D., Kyoto Prefectural University of Medicine
2003～2005	Guest Reseacher, Graduate School of Medicine, University of Tokyo, Japan
2004	Department of Ophthalmology, Kyoto Prefectural University of Medicine
2004～2006	Visiting Researcher, Osaka University, Osaka, Japan
2008～2011	Assistant Professor, Research Center for Inflammation and Regenerative Medicine, Faculty of Life and Medical Sciences, Doshisha University, Kyoto, Japan
2010～2015	Guest lecturer of Department of Ophthalmology, Kyoto Prefectural University of Medicine, Kyoto, Japan
2009～2011	Visiting Researcher, Osaka University, Osaka, Japan
2010	Guest Researcher, NIH, USA
2011～2015	Associate Professor, Research Center for Inflammation and Regenerative Medicine, Faculty of Life and Medical Sciences, Doshisha University, Kyoto, Japan
2011～2014	Guest Teacher, Osaka University, Osaka, Japan
2016～2018	Graduate student, Kenichi Ohmae Graduate School of Business
2018	MBA（Master of Business Administration）, Kenichi Ohmae Graduate School of Business
2012～present	Guest Reseacher, Graduate School of Medicine, University of Tokyo, Japan
2015.4～	Associate Professor, Kyoto Prefectural University of Medicine, Kyoto, Japan

LS5

Discovery by Simple Observation

John R. Stanley

Professor of Dermatology University of Pennsylvania, USA

Many great discoveries in medicine did not require genius, or even that much intelligence. They required only paying attention to simple observations. Examples from general medicine include the discovery of surgical anesthesia by Crawford Long；implantable eye lenses by Harold Ridley；and smallpox vaccination by Edward Jenner. An example from dermatology includes the discovery of the use of botox for wrinkles. Finally I will discuss, from my career, the discovery that pemphigus is an anti-desmosome autoimmune disease, and how staphylococcus causes blisters in order to circumvent the skin barrier in bullous impetigo.

Biography

Institution and Location	Degree	Completion Date	Field of Study
Cornell University, Ithaca, NY	B.A.	06/70	Physics
Harvard Medical School, Boston, MA	M.D.	06/74	Medicine
Internship（PGY-1）, Univ. of Washington, Seattle		7/74-6/75	Medicine
Residency, New York University		7/75-6/78	Dermatology
Postdoctoral fellowship, NIH, Bethesda		7/78-6/81	Cutaneous Biology

Positions and Employment

1981-1994	Assistant, Associate, and full Professor of Dermatology, Department of Dermatology, Uniformed Services University of the Health Sciences（USUHS）
1985-1994	Senior Investigator, Dermatology Branch, National Cancer Institute, NIH, Bethesda, MD
1/1995-11/2010	Professor and Chair, Department of Dermatology, University of Pennsylvania, Philadelphia, PA
2010-	Professor, Department of Dermatology, University of Pennsylvania, Philadelphia, PA

SCAR3-1

Pathomechanism of severe adverse drug reaction：Bench to Bedside

Riichiro Abe

Niigata University Graduate School of Medical and Dental Sciences, Japan

Stevens-Johnson syndrome（SJS）and toxic epidermal necrolysis（TEN）are rare, life-threatening mucocutaneous reactions characterized by extensive detachment of the skin. The eruptions can spread rapidly to the whole body within a day. We recently showed that keratinocyte death in SJS/TEN can be triggered by the interaction of annexin A1 and formyl peptide receptor（FPR）1 and may contribute to the pathogenesis of SJS/TEN. Annexin acts on FPR1, located on the surface of the skin cells, to cause necroptosis, a programed form of cell death. In addition I will introduce recent progress in of SJS/TEN pathomechanism.

Biography

Education

1988-1994	Hokkaido University School of Medicine

Degrees

1994	M.D., Hokkaido University School of Medicine
2001	Ph.D., Hokkaido University School of Medicine

Work Experience

1994-1998	Hokkaido University Graduate School of Medicine
1998-2000	Research fellow, Picower Institute for Medical Research
2000-2002	Staff dermatologist, Hokkaido University Graduate School of Medicine
2002-2007	Instructor, Hokkaido University Graduate School of Medicine
2007-2010	Assistant Professor, Hokkaido University Graduate School of Medicine
2010-2015	Associate Professor, Hokkaido University Graduate School of Medicine
2015-present	Professor, Niigata University Graduate School of Medical and Dental Sciences

SCAR3-2

Regulation of cytotoxic T cell in SJS/TEN

Wen-Hung Chung

Department of Dermatology, Drug Hypersensitivity Clinical and Research Center, Chang Gung Memorial Hospital, Taipei, Linkou and Keelung, Taiwan

Life-threatening severe drug hypersensitivity reactions, including Stevens-Johnson syndrome（SJS）and toxic epidermal necrolysis（TEN）, are known to cytotoxic T cell（CTL）-mediatedimmune disorders. We recently identified CTL-associated cytokines/cytotoxic proteins, such as IL-15 and granulysin, were significantly correlated with the disease severity in patients with TEN. More recently, we found the $CD4^+$ $CD25^+FOXP3^+$Treg population was significantly increased after anti-TNF-α treatment, which was also related to mortality in severe SJS/TEN. Understanding detailed immune pathomechanism will provide us not only the useful biomarkers for diagnosis and prevention but also therapeutic targets for treatments of SJS/TEN.

Biography

Dr. Chung is a physician of dermatology and a specialist of the field in severe cutaneous adverse drug reactions and cutaneous immunologic disorders. He currently serves as director of department of dermatology and drug hypersensitivity clinical and research center at Taipei & Linkou Chang Gung Memorial Hospital.

Dr. Chung has devoted himself into the investigation of severe adverse drug reactions（SCARs）for over a decade and his devotion and findings have great impact in clinic. Dr. Chung and his team has identified genetic and bio-markers for SCARs. He identified strong genetic association of HLA-B*1502 with carbamazepine-induced Stevens-Johnson syndrome（SJS）or toxic epidermal necrolysis（TEN）and HLA-B*5801 with allopurinol-SCARs. In addition, he also discovered granulysin as the major mediator for the extensive keratinocyte death in SJS or TEN. These important breakthroughs had been published on Nature and Nature Medicine in 2004 and 2008, respectively. These markers have been used in clinic before prescription of carbamazepine and allopurinol to prevent patients from the development of SCARs in many countries. Currently, Dr. Chung identified CYP2C variants, including CYP2C9*3 may reduce drug clearance, and play as the important genetic factors of phenytoin-related SCARs. The issue of drug metabolism or clearance has become an important risk factor for SCAR development. This important finding had been published on JAMA in 2014. Since these contributions, Dr. Chung had received awards, including 2009 the 47th Ten Outstanding Young Persons in Taiwan, 2011 the International League of Dermatological Societies（ILDS）Young Dermatologist International Achievement Award, and 2014 outstanding research award of Ministry of Science and Technology.

SCAR3-3

T cell receptor repertoire in Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis

Shuen-Iu Hung

Professor, Department and Institute of Pharmacology, School of Medicine, National Yang-Ming University, Taipei, Taiwan

Stevens-Johnson syndrome（SJS）and toxic epidermal necrolysis（TEN）are life-threatening severe cutaneous adverse reactions（SCAR）, which have the clinical manifestation of extensive skin necrosis. Cytotoxic T lymphocytes（CTL）have been proposed to play a key role in the pathogenesis of SJS/TEN, as the skin biopsies of SJS/TEN patients show CTL infiltration and blister fluid contains a lot of CTL and nature killer T cells producing cytotoxic proteins and cytokines, such as granulysin and IL-15. In addition, CTL are suggested to recognize the drug neoantigens in SJS/TEN, because some HLA alleles are genetic markers of SJS/TEN, and show binding affinity to the specific drug antigens. In this talk, I will present our recent studies of T cell receptor repertoire in SJS/TEN.

Biography

Education/Positions

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
Institute of Microbiology and Immunology, National Yang-Ming University, Taipei, Taiwan	PhD	1994-2002	Immunology
Institute of Biomedical Sciences, Academia Sinica, Taipei, Taiwan	Post-doc	2002-2003	Genomics
National Genotyping Center, Academia Sinica, Taipei, Taiwan	Assistant Director	2003-2006	Genomics
Institute of Pharmacology, National Yang-Ming University, Taipei, Taiwan	Assistant Professor	2006-2010	Immunopharmacology, Pharmacogenomics
Institute of Biomedical Sciences, Academia Sinica, Taipei, Taiwan	Adjunct Researcher	2009-2012	Genomics
Institute of Pharmacology, National Yang-Ming University, Taipei, Taiwan	Associate Professor	2010-2017	Immunopharmacology, Pharmacogenomics
Institute of Pharmacology, National Yang-Ming University, Taipei, Taiwan	Professor	2017-present	Immunopharmacology, Pharmacogenomics

SCAR3-4

Overview of effector cells and soluble mediators in SCARs

Teresa Bellón

Hospital La Paz Health Research Institute-IdiPAZ, Spain

Cutaneous adverse drug reactions are unpredictable and represent a number of skin diseases of varying degrees of severity. Those of most concern are usually referred to as severe cutaneous adverse reactions（SCARs）, and include acute generalized exanthematous pustulosis（AGEP）, drug reaction with eosinophilia and systemic symptoms（DRESS）, also known as drug-induced hypersensitivity syndrome or hypersensitivity syndrome（DIHS/HSS）, Stevens-Johnson's syndrome（SJS）, and toxic epidermal necrolysis（TEN）. All are delayed type IV hypersensitivity reactions in which a T cell-mediated drug-specific immune response is responsible for causing the disease. Nonetheless, specific T cell subpopulations develop in response to certain environments and produce cytokines that orchestrate the various phenotypes. Tc1, Th1, Th2, Th17, and Treg, among other T cell subpopulations, participate in the development of SCAR phenotypes. Cell subpopulations belonging to the innate immune system, comprising natural killer cells, monocytes, macrophages and dendritic cells, can also participate in shaping specific immune responses in various clinical entities.
Additionally, tissue resident cells including keratinocytes can contribute to epidermal damage by secreting chemokines that attract proinflammatory immunocytes. The final phenotypes in each clinical entity result from the interactions between a variety of cell types and their products.
Although the pathophysiology of these reactions is not fully understood, intensive research during recent years has led to major progress in our understanding of the contribution of certain cell types to the variability of SCAR phenotypes.

Biography

ACADEMIC BACKGROUND

University degree	*University*	*Date*
Biology	Universidad Complutense de Madrid	1987
PhD degree	*University*	*Date*
Biology	Universidad Autónoma de Madrid	1993

PREVIOUS RESEARCH EXPERIENCE

Position	*Institution*	*Date*
Graduate student	*Centro de Investigaciones Biológicas（CSIC）Spain*	*1987-1992*
Post-doctoral fellow	*Jefferson Cancer Institute（Philadelphia, PA）. USA*	*1993-1996*
Post-doctoral fellow	*Immunology Department -Hospital de la Princesa-Madrid, Spain*	*1996-2001*
Researcher	*Hosp. Universitario La Paz, Madrid Spain*	*2001-2007*

SCAR4-1

Cutaneous adverse reactions to cancer targeted therapies：What's new?

Chia-Yu Chu

Professor, Department of Dermatology, College of Medicine,
National Taiwan University, Taiwan

Dermatologic adverse events（dAEs）are common with the use of cancer targeted therapies, especially EGFR-TKI therapy. First- and second-generation agents（erlotinib, gefitinib, and afatinib）are frequently associated with acneiform rash, pruritus, xerosis, paronychia, and rarely, purpuric drug eruptions. The dAE profile is different with third-generation EGFR-TKIs. Osimertinib is associated with milder and less frequent dAEs than first-generation EGFR-TKIs, and therefore a different approach is warranted. Examples of other third-generation EGFR-TKIs will be also presented. Finally, dAE management approaches for EGFR-TKIs will be discussed.

Biography

EDUCATION：

M.D., National Taiwan University College of Medicine
Ph.D., Graduate Institute of Toxicology, National Taiwan University College of Medicine

POSTGRADUATE TRAINING & OCCUPATIONAL HISTORY：

1998-2002	Resident, Department of Dermatology, National Taiwan University Hospital, Taipei, Taiwan
2002-	Attending Doctor, Department of Dermatology, National Taiwan University Hospital, Taipei, Taiwan
2007-2008	Training for interviewer and reviewer, Dokumentationszentrum schwerer Hautreaktionen（dZh）, Universitäts-Hautklinik, University Medical Center Freiburg, Freiburg, GERMANY
2008-2013	Assistant Professor, Department of Dermatology, National Taiwan University College of Medicine
2008	Visiting Professor, Department of Dermatology, University of Paris（XII）, FRANCE
2008-2010	Clinical Research Fellow, Department of Dermatology, Henri Mondor Hospital, Paris, FRANCE
2013-2018	Associate Professor, Department of Dermatology, National Taiwan University College of Medicine

SCAR4-2

Self-specific T cells in anti-PD-1 treated NSCLC patients mediate autoimmune skin toxicity

Lukas Flatz

University of Zurich, Switzerland

Immunotherapy with checkpoint inhibitors targeting the PD-1/PD-L1 axis has shown promising results in cancer patients. However, autoimmune toxicity is frequent and ill understood. Here, we studied the pathophysiology of autoimmune skin toxicity in a prospective cohort of non-small cell lung cancer patients. We identified antigens found in NSCLC and healthy skin tissue by using a novel algorithm. Our data indicate that skin toxicity is associated with a good response to anti-PD-1 therapy. T cell clonotype analysis from paired lung and skin biopsies and T cell stimulation assays revealed shared specificities to tissue antigens that are likely representing the targets of both lung cancer regression and skin toxicity. These findings therefore highlight a potential mechanism of autoimmune skin toxicity, whereby the same T cell clonotypes with shared specificity for antigens in lung tumors and skin target both organs, leading to the development of skin-related side effects.
Furthermore, our data suggest that skin toxicity induced by anti-PD-1 therapy is related to treatment efficacy. It is likely that the relation to treatment efficacy depends on the organ to which the toxicity is targeted, as toxicities occurring in vital organs such as the heart are more likely to be fatal and will therefore not be associated with improved outcome. On the other hand, milder toxicities such as reported here may provide an opportunity to identify cancer T cell targets.

Biography

Lukas Flatz is a Swiss National Science Foundation professor at the University of Zurich and principal investigator at the Institute of Immunobiology at the Kantonsspital St.Gallen, Switzerland.
The current focus of his laboratory is to better understand T cell responses in checkpoint inhibitor treated patients. He established two prospective patient cohorts consisting of melanoma and of non-small cell lung cancer patients. Respective mouse models are used to confirm clinical findings. Before he established his own laboratory, he trained as a postdoc in the laboratory of Zinkernagel/Hengartner in Zurich and with Gary Nabel at the Vaccine Research Center at the National Institutes of Health in Bethesda, MD；USA. He did his residency in dermatology with Prof. Gilliet at the University of Lausanne. For more information go to：www.flatzlab.com.

SCAR4-3

Overlapping phenotypes in SCAR

Sylvia H Kardaun

Dept. Dermatology, Isala-Diaconessenhuis, Meppel, The Netherlands

Cases of SJS/TEN, AGEP and DRESS may share some features, complicating differentiation.
This raises the question whether these subtypes of SCAR present a continuum or that cases with overlap do exist. However, it makes sense to identify distinct entities rather than to consider the whole as a continuum, if it helps in finding original clinical patterns, courses, causes, mechanisms and treatment. This has resulted in the development of validation scoring systems for each SCAR subtype. Strict application of these scoring systems indicate that true overlap is rare.

Biography

EDUCATION

2012	PhD Medicine, University of Groningen Study of Severe Cutaneous Adverse Drug Reactions, challenges in diagnosis and treatment
1984	Specialized as dermatologist, University Medical Center Leiden
1978	MD Medicine, University Medical Center Groningen
1972	Teaching degree German language and culture, University of Groningen

WORK EXPERIENCE

2015-	Dept Dermatology Isala Diaconessenhuis, Meppel
2002-	Member RegiSCAR
1984-2015	Dept. Dermatology. University Medical Center Groningen Special areas of interest： - supervision and coaching residents Dept. Dermatology - dermatopathology - cutaneous adverse drug reactions - sexually transmitted diseases
2011-2015	Medical responsibility for all clinics of STD in the northern region of The `Netherlands
2011-2015	Member special taskforce STD NVDV
2008-2015	Member special taskforce eczema and allergology NVDV
2007-2015	Leader of Dutch Referral Center for Cutaneous Adverse Drug Reactions
2006-2018	Member Scientific Advisory Board of the Dutch Center for Pharmacovigilance Lareb
2003-2018	Reviewer and advisor WHO-Uppsala Monitoring Center Uppsala in the field of cutaneous adverse drug reactions

SCAR4-4

Pharmacogenomics of severe cutaneous adverse drug reactions in Thailand

Wichittra Tassaneeyakul

Department of Pharmacology, Faculty of Medicine, Khon Kaen University, Thailand

Severe cutaneous adverse drug reactions（SCARs）are rare but life-threatening. The causative drugs as well as genetic factors involved in SCARs may be varied in different ethnics. Results from our registration data base reveal that the most common causative drug of SCARs in Thailand was carbamazepine, allopurinol, phenytoin, co-trimoxazole and phenobarbital. Genetic factors involved in SCARs in a Thai population, particularly the genetic polymorphism of human leukocyte antigen（HLA）and cytochromes P450 genes will be discussed in this presentation.

Biography

Wichittra Tassaneeyakul obtained her B. Pharm from Faculty of Pharmaceutical Sciences, Chiang Mai University, Thailand and Master of Sciences in Pharmacology from Faculty of Sciences, Mahidol University, Thailand. She started her academic career as a lecturer in Department of Pharmacology, Faculty of Medicine, Khon Kaen University in 1987. She was awarded an Equity Merit Scholarship from Australian Government to study Ph. D. in Australia. She obtained her Ph.D. in the Department of Clinical Pharmacology, Flinders University of South Australia, Australia in 1994. She is now working as a head of department at Department of Pharmacology, Faculty of Medicine, Khon Kaen University, Thailand. Her research interests are pharmacogenomics, drug metabolism, pharmacokinetics and bioequivalence and biosimilar of pharmaceutical products. She has worked extensively in identifying genetic markers for prediction of drug-induced severe cutaneous reactions. She has published more than 70 papers in the international journals with high impact factor and had more than 2,500 citations for her publications.

SCAR4-5

TARC in drug reaction with eosinophilia and systemic symptoms/ drug-induced hypersensitivity syndrome（DRESS/DIHS）

Hideo Asada

Department of Dermatology, Nara Medical University School of Medicine, Japan

DRESS/DIHS is a severe drug-induced adverse reaction with fever, cutaneous eruptions, hematological abnormalities, organ dysfunction, and reactivation of HHV-6. Although management of DRESS/DIHS requires rapid diagnosis, it is difficult to distinguish the early phase of DIHS/DRESS from other forms of drug eruption. We observed that serum levels of TARC, a Th2-associated chemokine, were markedly higher in the acute stage of DIHS/DRESS than in other forms of drug eruption, and the levels correlated with clinical and immunological condition of DRESS/DIHS. These data suggest that TARC could be useful markers for early diagnosis and for assessing disease activity of DRESS/DIHS.

Biography

Education：

1984 MD in Nara Medical University

1989 PhD in Virology, Research Institute for Microbial Diseases, Osaka University

Professional Experience：

1989-1991	Medical Staff, Department of Dermatology, Minoo City Hospital
1991-1993	Senior Resident, Department of Dermatology, Osaka University Hospital
1993-1994	Assistant professor, Department of Dermatology, Osaka University School of Medicine
1994-1997	Visiting Fellow, Dermatology Branch, National Cancer Institute, NIH
1997-2000	Assistant professor, Department of Dermatology, Osaka University School of Medicine
2000-2002	Lecturer, Department of Dermatology, Osaka University School of Medicine
2002-2007	Associate professor, Department of Dermatology, Nara Medical University
2007-present	Professor, Department of Dermatology, Nara Medical University

SCAR5-1

Strontium ranelate-induced SCAR

Haur Yueh Lee [1,2]

[1] Head and Senior Consultant Dermatologist, Department of Dermatology, Singapore General Hospital（SGH）, Singapore
[2] Director, Allergy Centre, Singapore General Hospital, Singapore

Strontium ranelate is an anti-osteoporotic medication that was first registered in the European Union in 2004. Post marketing surveillance reports in Europe, suggested an increase risk with drug rash, eosinophilia and systemic symptoms and incidence of DRESS was estimated to be around 1/24,000 newly treated patients. Concurrently, reports of Stevens-Johnson syndrome and toxic epidermal necrolysis were reported particularly in Asian patients. HLA analysis of drug-tolerant controls as well as cases of Strontium-ranelate induced SJS/TEN suggested that HLA A*33：03 and B*58：01 are genetic risk factors for developing SJS/TEN in Asian patients.

Biography

Professional Qualifications

2011	Specialty certificate in Dermatology；Royal College of Physicians/British Association of Dermatology
2010	Fellow, Academy of Medicine（Dermatology）
2010	Advanced specialty training in Dermatology
2005	Member, Royal College of Physicians（MRCP）(United Kingdom）
	Masters of Medicine（Internal Medicine）NUS
2002	MBBS（National University of Singapore）

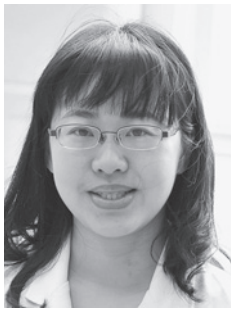
Working Experience

May 12 to Apr 17	Consultant, Department of Dermatology
May 10 to May 12	Associate Consultant, Dermatology Unit, SGH
May 08 to May 10	Registrar, National Skin Centre, Singapore
Nov 06 to May 08	Registrar, Dermatology Unit, SGH
May 03 to Nov 06	Medical Officer, Division of Medicine, SGH
May 02 to May 03	House Officer, Singapore Health Services

Academic Appointments

- Adjunct Assistant Professor, Duke-NUS Graduate Medical School.(2013 -)
- Clinical Senior Lecturer, National University of Singapore, Yong Loo Lin School of Medicine（2012 -）
- Clinical Physician Faculty Member, Family Medicine, Singhealth Residency Programme（2013-2015）
- Clinical Physician Faculty Member, Internal Medicine, Singhealth Residency Programme（2013-2015）

SCAR5-2



Endothelial injury associated with EGFR-TKIs

Yi-Shuan Sheen, Chia-Yu Chu

Department of Dermatology, National Taiwan University Hospital and College of Medicine, National Taiwan University, Taiwan

There are some reports of Epidermal growth factor receptor tyrosine kinase inhibitors（EGFR-TKIs）associated vascular adverse events. We revealed that EGFR-TKIs decreased the proliferation of HMEC-1s and HMVECs and also inhibited the MAPK pathway and EGFR phosphorylation. We found that increased IQGAP1 expression was associated with the decreased transendothelial electrical resistance and increased vascular permeability in vitro. Furthermore, IQGAP1 was over-expressed and colocalized in endothelial cells in the lesional skin.

Biography

Yi-Shuan Sheen is a lecturer at Department of Dermatology, College of Medicine, National Taiwan University. She received her M.D. degree from Kaohsiung Medical University and Ph.D. degree from the Graduate Institute of Pathology, National Taiwan University. Her research interests include melanoma, cancer biology, dermatologic surgery and laser.

SCAR5-3（SCAR-P1）

Combination of in-vivo and ex-vivo tests for drug causality assignment in severe cutaneous adverse drug reactions

Pawinee Rerknimitr[1], *Prattana Sittiwattanawong*[1], *Nattiya Hirankarn*[2], *Jettanong Klaewsongkram*[3]

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[2] Division of Immunology, Department of Microbiology, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand
[3] Division of Clinical Immunology, Department of Medicine, Faculty of Medicine, Skin and Allergy Research Unit, Chulalongkorn University, Bangkok, Thailand

Drug causality assessment in SCARs remains challenging. Available testing options include an in vivo drug patch test（DPT）and ex vivo interferon（IFN）-γ enzyme-linked immunospot（ELISpot）assay and lymphocyte transformation test（LTT）. DPT, ELISpot assays and LTT were performed in 30 patients with SCARs within the past 36 months. The tested drugs were chosen based on ALDEN and Naranjo scores. The positivity rate of drug patch test was 20%（n=6）. ELISpot assay yielded a positive result in 53%（n =16）while that of LTT was 42%（n=11）. By combining DPT and ELISpot, culprit drug assignment can be made in 73%（n=22）of the cases. ELISpot offered additional positivity especially with allopurinol. Therefore, combination of the tests may offer additional benefit in identifying the causative drugs.

SCAR5-4（P-1）
Induction of psoriasis on the scars following toxic epidermal necrolysis

Miho Mukai [1], Yuichi Kurihara [1,2], Hisashi Nomura [1], Yuka Shintani [1], Masayuki Amagai [1], Hayato Takahashi [1], Noriko Umegaki [1]

[1] Keio University Department of Dermatology
[2] Hiratsuka City Hospital

A 59-year old male with psoriasis for 2 years developed acute erythema and erosions on the whole body after taking a penicillin antibiotic, which was leading to toxic epidermal necrolysis（TEN）. The psoriatic lesions with scaly erythema appeared just on the scars due to TEN in two months. Then, psoriatic erythroderma and arthritis developed after treatment with percutaneous ethanol injection for hyperphosphatemia, which were improved by treatment with secukinumab. Re-epithelialization of severely affected lesion after TEN and ethanol injection might contribute to the characteristic course of psoriatic lesions in this case.

SCAR5-5

The Medication Risk of Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis in Asians

Tsu-Man Chiu

Director of Phototherapy, Division of Dermatology, Dept. Changhua Christian Hospital, Taiwan

Specific ethnic genetic backgrounds are associated with the risk of Stevens-Johnson syndrome/toxic epidermal necrolysis（SJS/TEN）especially in Asians. However, there have been no large cohort, multiple-country epidemiological studies of medication risk related to SJS/TEN in Asian populations. Thus, we analyzed the registration databases from multiple Asian countries who were treated during 1998-2017. A total 1,028 SJS/TEN cases were identified with the algorithm of drug causality for epidermal necrolysis（ALDEN）. Through the study, we establish risk profiles for medications related to SJS/TEN in Asians.

Furthermore, those medications labeled by the US Food and Drug Administration（FDA）as carrying a risk of SJS/TEN were also compared with the common causes of SJS/TEN in Asian countries. We also compare risk profiles to those for European populations. Oxcarbazepine, sulfasalazine, COX-II inhibitors, and strontium ranelate were identified as new potential causes. In addition to sulfa drugs and beta-lactam antibiotics, quinolones were also a common cause. Only one acetaminophen-induced SJS was identified, while several medications（e.g., oseltamivir, terbinafine, isotretinoin, and sorafenib）labeled as carrying a risk of SJS/TEN by the FDA were not found to have caused any of the cases in the Asian countries investigated in this study.

Biography

Education

2009-2011	Master of Medicine, Institute of Medicine；Chung Shan Medical University
1990-1997	MD, Department of Medicine；Chung Shan Medical University

Appointments Held

2010-	Director, Division of Phototherapy, Department of Dermatology, Changhua Christian Hospital
2002-2009	Attending Doctor, Department of Dermatology, Changhua Christian Hospital
2001-2002	Fellow, Department of Dermatology, Changhua Christian Hospital
1997-2001	Resident, Department of Dermatology, Changhua Christian Hospital

SCAR5-6

Major Psychological Complications and Decreased Health-Related Quality of Life among Survivors of Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis

R P Dodiuk-Gad [1,2], C. Olteanu [3], A. Feinstein [4], R. Hashimoto [1], R. Alhusayen [1], S. Whyte-Croasdaile [5], Y. Finkelstein [6], M. Burnett [7], S. Sade [8], R. Cartotto [7], M.G. Jeschke [7], N.H. Shear [1,9]

[1] Division of Dermatology, Department of Medicine, Sunnybrook Health Sciences Centre, University of Toronto, Toronto, Canada
[2] Department of Dermatology, Ha'emek Medical Center, Afula, Israel
[3] Faculty of Medicine, University of Toronto, Toronto, Canada
[4] Department of Psychiatry, Sunnybrook Health Sciences Centre, Toronto, Canada
[5] SJS and TENS Group Canada-CAST International, Toronto, Canada
[6] Paediatric Emergency Medicine, Clinical Pharmacology and Toxicology, The Hospital for Sick Children, Toronto, Canada
[7] Ross Tilley Burn Centre, Sunnybrook Health Sciences Centre, Toronto, Canada
[8] Department of Pathology, Sunnybrook Health Sciences Centre, Toronto, Canada
[9] Division of Clinical Pharmacology and Toxicology, Department of Medicine, Sunnybrook Health Sciences Centre, Toronto, Canada

Introduction
Stevens-Johnson Syndrome（SJS）and Toxic Epidermal Necrolysis（TEN）are life-threatening mucocutaneous reactions.
Methods
Survivors of SJS/TEN were assessed using validated questionnaires and one designed for this study to assess their psychological complications and health-related quality of life.
Results
Eleven of 17（65%）participants were found to have symptoms of post-traumatic stress, 12（71%）had psychological distress, and 11（65%）had symptoms of a psychiatric disorder. A moderate-extremely large effect on the lives of 9（53%）participants was found. Fourteen（82%）participants reported that SJS/TEN decreased their quality of life.
Conclusions
Survivors suffer from severe long-term psychological complications and decreased health-related quality of life.

SCAR5-7

Severe Physical Complications among Survivors of Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis

C. Olteanu [1], N.H. Shear [2,3], H.F. Chew [4], R. Hashimoto [2], R. Alhusayen [2], S. Whyte-Croasdaile [5], Y. Finkelstein [6], M. Burnett [7], M. Ziv [8], S. Sade [9], M.G. Jeschke [7], R.P. Dodiuk-Gad [2,8]

[1] Division of Dermatology, Department of Medicine, University of Alberta, Edmonton, Canada
[2] Division of Dermatology, Department of Medicine, Sunnybrook Health Sciences Centre, University of Toronto, Toronto, Canada
[3] Division of Clinical Pharmacology and Toxicology, Department of Medicine, Sunnybrook Health Sciences Centre, Toronto, Canada
[4] Department of Ophthalmology and Vision Sciences, Sunnybrook Health Sciences Centre, Toronto, Canada
[5] SJS and TENS Group Canada, CAST International, Toronto, Canada
[6] Paediatric Emergency Medicine, Clinical Pharmacology and Toxicology, The Hospital for Sick Children, Toronto, Canada
[7] Ross Tilley Burn Centre, Sunnybrook Health Sciences Centre, Toronto, Canada
[8] Dermatology Department, Emek Medical Center, Bruce Rappaport Faculty of Medicine, Technion-Institute of Technology, Haifa, Israel
[9] Department of Pathology, Sunnybrook Health Sciences Centre, Toronto, Canada

Introduction
Stevens-Johnson Syndrome（SJS）and Toxic Epidermal Necrolysis（TEN）are the most severe types of cutaneous adverse reactions to drugs.
Method
Survivors older than 18 years were assessed by an interview and by skin, oral mucous membrane and ophthalmic exam.
Results
Of 17 patients, the most common cutaneous sign was post-inflammatory dyspigmentation（77%）and the most common cutaneous symptom was pruritus（53%）. Dry eyes were the most common ophthalmic finding（44%）. Hair loss and nail loss were reported in 53% and 35% of participants, respectively.
Conclusions
Survivors of SJS/TEN suffer from severe, long-term physical complications and require ongoing medical follow-up.

SCAR6-1

Drug eruption resembling drug-induced hypersensitivity syndrome developed 5 months after starting on lamotrigine

Anna Nakajima, Yuka Sugano, Kohei Ogawa, Fumi Miyagawa, Hiroaki Azukizawa, Hideo Asada

Nara Medical University, Japan

A 72-year-old male noticed erythema on his body one week previously. Physical examination at our department revealed edematous erythema on his face, pallor around the eyes, papules, pustules, and desquamation around the mouth, and pale erythema on the trunk and extremities. Administration of levetiracetam, nifedipine, and lamotrigine was initiated from over 5 months ago.We suspected drug-induced hypersensitivity syndrome due to lamotrigine and discontinued the drug. However, the eruptions got worse and it took three weeks until they completely resolved. Laboratory test showed eosinophilia, elevated levels of serum TARC and reactivation of HHV-6. Although this case did not satisfy the diagnostic criteria for DIHS, a similar pathological condition to DIHS might be involved in this patient.

SCAR6-2（SCAR-P6）
Cytomegalovirus skin ulcer in drug-induced hypersensitivity syndrome

Tatsuya Katsumi, Yuuki Iwai, Koichi Tomii, Takeo Suzuki, Tokiko Deguchi, Yoya Shigehara, Atsushi Fujimoto, Riichiro Abe

Department of Dermatology, Niigata University Graduate School of Medical and Dental Sciences, Niigata, Japan

Drug-induced hypersensitivity syndrome（DIHS）is one of a severe cutaneous adverse drug reactions. It is characteristic that various human herpesviruses reactivation, especially cytomegalovirus（CMV）occurs in DIHS patients. Reactivation of CMV in DIHS patients induces small skin ulcer. In our case, when the small skin ulcer appeared, CMV antigen was not detected in peripheral blood leukocytes. After 14 days, CMV antigen became positive. In DIHS patient, small skin ulcer could be the initial sign of CMV infection before CMV antigen became positive.

SCAR6-3

Severe Cutaneous Adverse Drug Reactions（SCARs）in Malaysia

Siew Eng Choon

Hospital Sultanah Aminah Johor Bahru, Johor, Malaysia

Reliable data on SCARs are mainly based on case series reported by dermatology departments of various hospitals throughout Malaysia. Steven-Johnson Syndrome/Toxic epidermal necrolysis（SJS/TEN）spectrum is the most common SCAR reported followed by Drug Rash with Eosinophilia and Systemic Symptoms（DRESS）, Acute Generalized Exanthematous Pustulosis and generalized Fixed Drug Eruptions. Commonly implicated drugs are allopurinol, anti-convulsants, namely phenytoin and carbamazepine, antibiobitics（cotrimoxazole, dapsone, aminopenicillns）and NSAID mainly mefenamic acid. Mortality rate for TEN,SJS and DRESS was as high as 20% and 12% respectively.

Biography

Dr. Choon Siew Eng is a senior consultant dermatologist at Hospital Sultanah Aminah, Johor Bahru, Malaysia and Associate Professor, Clinical School Johor Bahru, Jeffrey Cheah School of Medicine and Health Sciences, Monash University, Malaysia. She received her medical degree from the University of Malaya. She subsequently undertook postgraduate training in general medicine and obtained membership of the Royal College of Physicians（London, UK）and was elected a fellow in 2003. She was awarded a public service scholarship to pursue dermatology training and subsequently a fellowship to train in dermatopathology in St. John's Institute of Dermatology, London, UK.

She is involved in medical undergraduate teaching and supervises postgraduate dermatology trainees for the Advanced Diploma in Dermatology. Dr. Choon is a foundation member of Asian Academy of Dermatology and Venereology and an active member of the Malaysian Society of Dermatology as well as a member of the Malaysian Medical Association. Her research interests include psoriasis particularly pustular psoriasis and cutaneous adverse drug reactions. She was recently elected as a councilor for the International Posriasis Council, a global non-profit organisation, dedicated to improving care of people living with psoriasis through research and education. Dr. Choon has authored and/or co-authored more than 70 peer-reviewed articles and has contributed chapters to various other publications.

SCAR6-4

Combined therapy of TNF-alpha antagonist and systemic steroids for SJS/TEN

Chun-Wei Lu

Department of Dermatology, Drug Hypersensitivity Clinical and Research Center, Chang Gung Memorial Hospital, Linkou, Taiwan

Cytotoxic T lymphocyte-mediated (CTL-mediated) severe cutaneous adverse reactions (SCARs), including Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), are rare but life-threatening adverse reactions commonly induced by drugs. Although high levels of CTL-associated cytokines, chemokines, or cytotoxic proteins, including TNF-α and granulysin, were observed in SJS-TEN patients in recent studies, the optimal treatment for these diseases remains controversial. In our previous study, we had evaluated the efficacy, safety, and therapeutic mechanism of a TNF-α antagonist in CTL-mediated SCARs. Now we trying to know whether TNF-α antagonist combined systemic steroid could be a more efficient choice of CTL-mediated SCARs.

Biography

Education：

2004-2011 School of Medicine, Medical School of Tzu Chi University (M.D.)

Post-Graduate Education：

2017- Graduate Institute of Clinical Medical Science of Chang-Gung University, Candidate of Ph.D

Employment Record：

2012-2016 Resident, Department of Dermatology, Chang Gung Memorial Hospital, Linkou, Taiwan

2016- Attending, Department of Dermatology, Chang Gung Memorial Hospital, Linkou, Taiwan

2017- Consultant of Taiwan Severe Cutaneous Drug Reaction Association

2017- Deputy secretary general of Taiwan Evidance Based Medicine Association

SCAR6-5

Lupus erythematosus-associated epidermal necrolysis mimicking Stevens-Johnson syndrome and toxic epidermal necrolysis

Chun-Bing Chen

Department of Dermatology, Drug Hypersensitivity Clinical and Research Center, Chang Gung Memorial Hospital, Keelung, Taipei, Linkou, Chang Gung University College of Medicine, Taoyuan, Taiwan

Stevens-Johnson syndrome（SJS）and toxic epidermal necrolysis（TEN）are considered a spectrum of life-threatening idiosyncratic reactions, primarily induced by medications. Rarely, lupus erythematosus have been reported to cause SJS/TEN. Erythema multiforme（EM）-like, subepidermal blisters, SJS/TEN-like lesions can occur in patients with lupus erythematosus. Rowell et al. first described EM-like eruptions in the setting of systemic lupus erythematosus. Epidermal necrolysis can develop as a result of immune reactant accumulation or dermal vasculitis at the basal membrane of the skin. LE patients mimicking EM, SJS and TEN is a specific cutaneous manifestation of lupus erythematosus. Longer clinical course, positive ANA, decreased C3 or C4, positive lupus band test, and periadnexal infiltration or melanin incontinence in histopathology help to differentiate from classical EM or drug-related epidermal necrolysis.

Biography

Doctor Chun-Bing Chen received his medical degree from the Chang Gung Memorial Hospital. He received one year residency training in the Department of Medicine in Taipei Veterans General Hospital. He subsequently completed his residency and fellowship training in the Department of Dermatology in Chang Gung Memorial Hospital. He went on to obtain his PhD in Graduate Institute of Clinical Medical Sciences in Chang Gung University.

Doctor Chen is an active physician of dermatology and consultant of Drug Hypersensitivity Clinical and Research Center, and Immune-Oncology Center of Excellence in Chang Gung Memorial Hospital. He also worked as Lecturer of the department Dermatology at Chang Gung Memorial Hospital. His research interest focus on severe cutaneous adverse reactions, immune-related adverse events, cutaneous immunological disorders and pharmacogenomics.

SCAR6-6（P-2）

The thymus and activation-regulated chemokine（TARC）level in serum at an early stage of a drug eruption is a prognostic biomarker of severity of systemic inflammation

Takayoshi Komatsu-Fujii[1], *Yuko Chinuki*[2], *Hiroyuki Niihara*[2], *Kenji Hayashida*[2], *Masataka Ohta*[2], *Sakae Kaneko*[2], *Eishin Morita*[2]

[1] Department of Dermatology, Kyoto University School of Medicine, Kyoto, Japan
[2] Department of Dermatology, Shimane University Faculty of Medicine, Shimane, Japan

Background：In severe drug eruptions, precise evaluation of disease severity at early stages is difficult. We aimed to test whether serum thymus and activation-regulated chemokine（sTARC）levels at early stages can serve as a prognostic biomarker of drug eruptions.
Methods：Study participants included 81 patients（drug rash with eosinophilia and systemic symptoms, maculopapular exanthema, and erythema multiforme）. We evaluated sTARC levels at the first visit and calculated correlation between sTARC and inflammatory scores, including CRP and systemic inflammatory response syndrome（SIRS）score.
Results and conclusion：sTARC levels positively correlated with inflammatory scores, suggesting prognostic value of sTARC for drug eruptions.

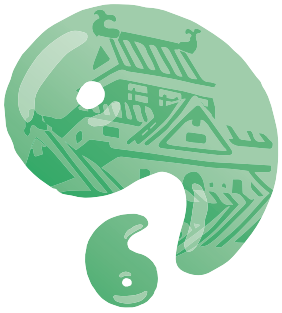
SCAR6-7

Rapid detection of HLA-A*3101 and HLA-B*5801 by Loop mediated isothermal amplification（LAMP）

Hiroyuki Niihara, Kunie Kohno, Eishin Morita

Department of Dermatology, Shimane University Faculty of Medicine, Shimane, Japan

The relation between a specific HLA and a causative drug of adverse drug eruption（ADE）has been revealed in a recent decade. Detecting HLA related to an ADE is effective to identify a causative drug. However, the HLA typing cost high and is time consuming. Loop mediated isothermal amplification（LAMP）has recently been recognized as an effective tool to detect specific SNP. We apply LAMP to detect HLA-A*3101 related to carbamazepine-induced ADE or HLA-B*5801related to allopurinol-induced ADE.



Poster Presentation

The 10th International Congress on Cutaneous Adverse Drug Reactions

iSCAR 2018

SCAR-P1（SCAR5-3）
Combination of in-vivo and ex-vivo tests for drug causality assignment in severe cutaneous adverse drug reactions

Pawinee Rerknimitr[1], *Prattana Sittiwattanawong*[1], *Nattiya Hirankarn*[2], *Jettanong Klaewsongkram*[3]

[1] Division of Dermatology, Department of Medicine, Faculty of Medicine, Skin and Allergy Research Unit, Chulalongkorn University, Bangkok, Thailand
[2] Division of Immunology, Department of Microbiology, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand
[3] Division of Clinical Immunology, Department of Medicine, Faculty of Medicine, Skin and Allergy Research Unit, Chulalongkorn University, Bangkok, Thailand

Drug causality assessment in SCARs remains challenging. Available testing options include an in vivo drug patch test（DPT）and ex vivo interferon（IFN）-γ enzyme-linked immunospot（ELISpot）assay and lymphocyte transformation test（LTT）. DPT, ELISpot assays and LTT were performed in 30 patients with SCARs within the past 36 months. The tested drugs were chosen based on ALDEN and Naranjo scores. The positivity rate of drug patch test was 20%（n=6）. ELISpot assay yielded a positive result in 53%（n =16）while that of LTT was 42%（n=11）. By combining DPT and ELISpot, culprit drug assignment can be made in 73%（n=22）of the cases. ELISpot offered additional positivity especially with allopurinol. Therefore, combination of the tests may offer additional benefit in identifying the causative drugs.

SCAR-P2
Proportion of circulating dendritic cells is decreasing in patients with severe cutaneous adverse drug reaction.

Naoko Takamura, Yukie Yamaguchi, Tomoya Watanabe, Yuko Watanabe, Michiko Aihara

Department of Environmental Immuno-Dermatology, Yokohama City University Graduate School of Medicine, Yokohama, Japan

Drug eruptions are thought to be induced by T cells that have been sensitized by dendritic cells. We investigated circulating and skin infiltrating dendritic cells（DCs）in severe drug eruption patients to clarify whether they differ according to the disease type. We found that the proportion of circulating DCs in patients with Toxic epidermal necrolysis（TEN）, Stevens-Johnson Syndrome, drug-induced hypersensitivity syndrome/drug reaction with eosinophilia and systemic symptoms was significantly decreased in the acute phase compared to that in healthy subjects, and circulating myeloid DC levels in TEN patients tended to be lower than in the other disease types.

SCAR-P3
Influence of aromatic antiepileptic drug binding on the peptide repertoire of HLA-B*15：02

Ryosuke Nakamura [1], *Yoshimi Okamoto-Uchida* [1], *Noritaka Hashii* [2], *Noriaki Arakawa* [1], *Yumiko Matsuzawa* [1], *Akiko Ishii* [2], *Yoshiro Saito* [1]

[1] Division of Medicinal Safety Science, National Institute of Health Sciences, Kawasaki, Japan
[2] Division of Biological Chemistry and Biologicals, National Institute of Health Sciences, Kawasaki, Japan

［Aim］Some kind of drug is known to alter the HLA-presenting peptide repertoire. We aimed to determine whether binding of aromatic antiepileptic drugs with HLA-B*15：02 would also induce the peptide repertoire alteration.
［Methods］ Soluble tagged HLA-B*15：02 molecules were produced in HLA-deficient B cells that were treated with carbamazepine, oxcarbazepine, and phenytoin for 2 weeks. HLA-binding peptides were purified, and analyzed with LC-MS/MS.
［Results］More than 1,000 unique peptides were detected in each condition. We found significantly more short peptides（5 mer） after the drug treatments. Such short peptides may play important roles in the pathogenesis of idiosyncratic skin reactions.

SCAR-P4
IP-10/CXCR3 axis participates to a different extent in the skin inflammatory process of DRESS and SJS/TEN

Che-Wen Yang [1,2], *Chia-Yu Chu* [2]

[1] Department of Dermatology, Cathay General Hospital, Taiwan
[2] Department of Dermatology, National Taiwan University Hospital and National Taiwan University College of Medicine, Taiwan

Published studies have indicated that drug reaction with eosinophilia and systemic symptom（DRESS）is a drug-specific immune response, thus making it valuable to identify specific biomarkers. Even though there is currently no universally accepted biomarker, previous reports had found that CXCL10, also known as interferon γ-induced protein-10（IP-10） may participate in the pathogenesis of cutaneous adverse drug reactions. In our prospective study, more abundant IP-10$^+$ and CXCR3$^+$ cells were demonstrated in DRESS skin biopsies on immunohistochemistry analysis. Also, there were significantly higher percentage of skin-homing CXCR3$^+$CD4$^+$ T cells and CXCR3$^+$CD8$^+$ T cells in the PBMCs of patients of DRESS.

SCAR-P5
Acute generalized exanthematous pustulosis caused by hydroxychloroquine

Marie Suzuki, Yusuke Saruta, Yuka Kato, Hideaki Watanabe, Hirohiko Sueki

Department of Dermatology, Showa University Faculty of Medicine, Tokyo, Japan

A 66-year-old woman presented with pustular rash. The patient fulfilled diagnostic criteria for systemic lupus erythematosus（SLE）and received treatment with 200 mg/day hydroxychloroquine, 2.5 mg/day prednisolone, and 150 mg/day cyclosporine A. High fever and generalized erythematous plaques with disseminated pustules developed 18 days after commencement of treatment. Laboratory data showed leukocytosis, neutrophilia and accelerated erythrocyte sedimentation. Biopsy revealed spongiform intraepidermal pustules and perivascular lymphocytic infiltration. Lymphocyte stimulation test was negative. The diagnosis was acute generalized exanthematous pustulosis（AGEP）. Hydroxychloroquine was withdrawn and 30 mg/day of systemic prednisolone was started. Erythema and pustular lesions resolved completely within 14 days.

SCAR-P6（SCAR6-2）
Cytomegalovirus skin ulcer in drug-induced hypersensitivity syndrome

Tatsuya Katsumi, Yuuki Iwai, Koichi Tomii, Takeo Suzuki, Tokiko Deguchi, Yoya Shigehara, Atsushi Fujimoto, Riichiro Abe

Department of Dermatology, Niigata University Graduate School of Medical and Dental Sciences, Niigata, Japan

Drug-induced hypersensitivity syndrome（DIHS）is one of a severe cutaneous adverse drug reactions. It is characteristic that various human herpesviruses reactivation, especially cytomegalovirus（CMV）occurs in DIHS patients. Reactivation of CMV in DIHS patients induces small skin ulcer. In our case, when the small skin ulcer appeared, CMV antigen was not detected in peripheral blood leukocytes. After 14 days, CMV antigen became positive. In DIHS patient, small skin ulcer could be the initial sign of CMV infection before CMV antigen became positive.

SCAR-P7

B cell depletion precede human herpesvirus 6 reactivation in patients with drug reaction with eosinophilia and systemic symptoms（DRESS）

Po-Wei Huang[1], *Che-Wen Yang*[1,2], *Chia-Yu Chu*[1]

[1] Department of Dermatology, National Taiwan University Hospital and National Taiwan University College of Medicine, Taiwan
[2] Department of Dermatology, Cathay General Hospital, Taiwan

Drug reaction with eosinophilia and systemic symptoms（DRESS）is a drug related, multi-organ involved severe cutaneous adverse reaction. Its pathogenesis is not fully established. It has been proposed that hypogammaglobulinemia and B cell depletion may lead to HHV-6 reactivation and DRESS. However, not all DRESS patients had HHV-6 reactivation in most of the studies. We conducted a prospective study of 36 DRESS patients and 25 SJS patients. The frequency of B cell depletion was observed more commonly in DRESS cases than in SJS/TEN cases. The B cell count was significantly lower in DRESS than in SJS/TEN and also in HHV-6 reactivated DRESS compared to HHV-6 non-reactivated DRESS.

SCAR-P8

A current review of reported genetic associations with cutaneous adverse drug reactions and recommendations on genetic screening for their prevention

Felix L. Chan[1], *Neil H. Shear*[2], *Roni P. Dodiuk-Gad*[3,4]

[1] Mississauga Academy of Medicine, Faculty of Medicine, University of Toronto, Mississauga, ON, Canada
[2] Division of Dermatology, Department of Medicine, Sunnybrook Health Sciences Centre, University of Toronto, Toronto, ON, Canada
[3] The Ruth and Bruce Rappaport Faculty of Medicine, Technion Institute of Technology, Israel
[4] Department of Dermatology, Emek Medical Centre, Israel

An up-to-date and thorough review of MEDLINE-indexed literature regarding genetically-associated cutaneous adverse drug reactions（CADRs）, was conducted. Genetic associations to CADRs were reported based on relevance to dermatology, statistical significance, and scientific consensus. The data was organized by pharmacological class, drug, genetic association, type of cutaneous reaction, and ethnic population affected. Sensitivities, specificities, and positive and negative predictive values of genetic associations to CADRs were included when available. Current recommendations on genetic screening to prevent CADRs, including various national guidelines, were summarized and organized according to drug, genetic association, and source.

SCAR-P9

Antibiotics use and risk of severe, life-threatening adverse reactions.
（An international collaborative study between Canada and Taiwan）

Wan-Chun Chang [1,2], Chuang-Wei Wang [3,4], Shuen-Iu Hung [5], Wen-Hung Chung [3,4,6], Bruce C. Carleton [1,2]

[1] Division of Translational Therapeutics, Department of Pediatrics, Faculty of Medicine, University of British Columbia, Vancouver, British Columbia, Canada
[2] British Columbia Children's Hospital Research Institute, Vancouver, British Columbia, Canada
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Antibiotics have saved hundreds of millions of lives；however, antibiotics are also one of the most common offenders of adverse drug reactions（ADRs）ranging from common rash to rare, serious systemic reactions, including anaphylaxis and severe cutaneous adverse reactions（SCARs）. Unlike what was found in previous studies of antiepileptic medicines, the genetics behind antibiotic-related severe ADRs appears more heterogeneous across different populations. Dr. Bruce Carleton at UBC in Canada and Dr. Wen-Hung Chung in CGMH in Taiwan aim to establish an international clinical and genetic database, which will provide a comprehensive platform offering pharmacogenomics data sharing and knowledge translation.

SCAR-P10

Short course of cyclosporine A as a treatment option for drug-induced hypersensitivity syndrome：3 cases and review of the literature.

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Background：Drug-induced hypersensitivity syndrome is characterised by unique skin manifestations and serious extracutaneous organ dysfunction associated with herpesvirus reactivation. Although administration of high-dose corticosteroids is empirically recommended, whether it is appropriate as the first-line treatment of DIHS/DRESS remains controversial. **Objective**：To evaluate cyclosporine A therapy as an optional treatment of DIHS/DRESS. **Methods**：We described three cases of DIHS/DRESS treated with a short course of CyA and review the relevant literature. **Results**：These cases were administered CyA for ≤7 days, resulting in complete regression without relapse or sequelae.