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### Scientific Report

### Wound Healing 2016

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Meeting Report from the Euroscicon event: 26th – 28th January 2016, London UK Meeting Chairs: Professor Steven Percival, 5D Health Protection Group Ltd and University of Liverpool, UK

Dr Narendra Kumar, Associate Professor (Tenured), Department of Pharmaceutical Sciences, TX, USA Dr Andrew Tee, Senior Lecturer in Cancer Genetics, Cardiff University, UK Dr Zhi-Ren Liu, Georgia State University, USA

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### Abstract

The 2016 Wound Healing conference was held over three days in London, United Kingdom. This inaugural interdisciplinary event provided a platform for various speakers to present both scientific and clinical research and novel technologies relevant to wound healing. The meeting aimed to promote discussion and debate from international views in an informal setting to deliver updates in the most front-line advances of wound healing. A wide variety of subjects were discussed including biofilm management, copper, reactive oxygen species and non-thermal gas plasma. The meeting report will summarise a selection of the presented topics as well as document abstracts from the topics and posters that were presented.

### Introduction

The Wound healing 2016 conference was held in London and organised by EuroSciCon. Attended by various researchers and clinicians, the event covered different aspects of wounds ranging from laboratory-based research to clinical assessment of wounds, covering the whole healing pathway. The research was presented on the biochemical pathways and dressings management for infection control and healing improvement. Drawing from inter-disciplinary experiences, the event provided an open forum to discuss and examine novel ways to promote wound healing and management including pharmacological, surgical strategies and new concepts such as antibiofilm agents.

The first day focused on managing infections and was chaired by Professor Steven Percival (5D Health Protection Group Ltd. and University of Liverpool, UK). On the second day, Dr Narendra Kumar (Texas A& M Rangel College of Pharmacy, Texas) chaired the first session on stem cells and regeneration. The second session discussed wound healing stimulation and was chaired by Dr Andrew Tee (Cardiff University, UK). The final day discussed fibroblasts and myofibroblasts in wound healing, chaired by Dr ZhiRen Liu (Georgia State University, USA).

**Speakers Summaries Biofilms: A Paradigm Shift in Wound Microbiology** *Professor Steven Percival, 5D Health Protection Group Ltd* 

### and University of Liverpool, UK

Professor Percival discussed the formation and importance of the microbiology and biofilms in chronic cutaneous wounds. He highlighted that microbes within chronic wounds reside in two phenotypic states, either a planktonic (free-floating) or as a biofilm (sessile) state. The predominant microbial state within the wound environment is the attached or sessile state [1]. The human body supports several different microbiotas, which

are composed of a diverse range of microorganisms. These microbes can disseminate and colonise new surfaces. One such surface is a cutaneous wound where exogenous and endogenous microbes can grow as a biofilm, which can increase a wound propensity to a localised and potential systemic infection. Initially, within the wound environment, gram-positive bacteria adhere to the wound surface and over several weeks as the complexity of the microbial environment changes, gramnegative bacteria, anaerobes and fungi begin to populate. These microbes migrate deeper into the wound, and phenotypically exhibit fastidious requirements. Consequently, when routine swabbing of a wound is undertaken, these wound swabs fail to recover this microbial population, within the biofilm state, and are often culture negative. Therefore, to obtain representative samples to determine the microbiology of a wound aspirates or biopsies are better techniques to assess the wound flora.

Biofilms within the wound are composed of low levels of microorganisms which are immobilised within a matrix of Extracellular Polymeric Substances (EPS). These biofilms can be found in different regions of the wound environment i.e. wound bed, slough, necrotic tissue and wound dressing. As microbes within the biofilm proliferate, they adapt to the chronic wound environment increasing their tolerance to antimicrobials and the immune response, eventually disseminating to other sites of the human body leading to systemic infection.

The management of wounds is significant for supporting the wound healing process. Many of these wound dressings incorporate antimicrobial agents with the aim to control the microbial burden in wounds that are at risk of or clinically infected. The most widely used antimicrobial in wound care is silver which is effective when present in its ionic form. However, there is an urgent need for more advanced antimicrobials that are effective on microbes growing within the biofilm phenotypic state. Professor Pervical discussed the option of treating the different biofilms within the wound environment and the approaches which could lead to a potential positive clinical outcome.

### Mechanism of wound repair in gastrointestinal tract

Dr. Narendra Kumar, Associate Professor (Tenured), Department of Pharmaceutical Sciences, TX, USA

Dr Kumar presented his researches on the expression of Jak3 and its implication on mucosa wound repair and homeostasis. The human gut is a huge surface area (50-110 times greater than the area of skin), approximately 260-300m2. It is also the part of the body most exposed to the environment. Injuries and inflammation of the intestinal mucosa are frequent; because of this, 60% of the immune system is concentrated in the gut.

Janus kinase 3 (Jak3) is a non-receptor tyrosine kinase expressed in both hematopoietic and non-hematopoietic cells. It is known to play essential roles in cytoskeletal remodelling, epithelial wound healing and mucosa homeostasis through interactions with cytoskeletal and adapter proteins. Dr Kumar and his research team found that Jak3 expression was essential for differentiation, mucin expression and barrier functions of the colonic mucosa, which are essential for the protection of the mucosal surfaces. Abnormal activation of Jak3 was associated with human haematological and epithelial malignancies. Showing that a tight balance in Jak3 activity is essential for normal hematopoietic development and epithelial functions [2].

In his study, they characterised the role of Jak3 on mucosa differentiation, colonic inflammation and structural changes in mucosal surfaces of the colon as well as demonstrating the mechanism of Jak3-mediated mucosal differentiation, where Jak3 regulated the expression of differentiation markers, formation of mucus in mice and facilitated barrier functions through its interactions and adherens junction (AJ) localisation of beta-catenin in human Intestinal epithelial cells [3].

Jak3 influences the cytoskeleton by attaching to the protein villin and induces remodelling. Its co-ordinates cells migration, cell survival, cell proliferation and cell differentiation. Once activated, Jak3 attaches to the cell membrane leading to redistribution of actin filaments and increasing some of the wound repair mechanisms [4].

Dr Kumar and his team also worked on the mechanisms through which Jak3 regulates mucosa tolerance, chronic lowgrade inflammation and associated metabolic syndrome. They found that the loss of Jak3 leads to increased body weight in mice and also increased basal chronic low-grade inflammation of the gastrointestinal tract [5].

### Management of diabetic foot healing: experience of the national centre of burns and plastic surgery: Morocco

Dr Rafik Amine, Resident in Plastic surgery, National Center for Burns and Plastic Surgery, Casablanca, Morocco

Dr Amine Rafik presented a retrospective clinical study conducted in the Moroccan National Burns and Plastic surgery centre on the management of diabetic foot ulcers and surgical soft tissue closure of severe diabetic foot infections.

He highlighted the fact that patients' education is a major component of adequate wound care as a delayed presentation may lead to amputation. More than half (60%) of the cohort presented with a grade III-IV of the Wagner grading system for diabetic foot infection, and 52% of the treated patients had radiological signs of osteomyelitis. One third of the patients had positive microbiology culture. The treatment options were debridement (76%), skin graft/ integra (84%) and amputation (24%). Among the cohort, infection recurrence rate was 10% and secondary amputation was performed on 12% of the treated patients.

This high rate of advanced diabetic foot infection is long standing in diabetes, delayed presentation, poorly managed diabetes and poorly managed wounds, highlighting a lack in communication.

Dr Rafik's team discussed the different treatment options such as hyperbaric oxygen therapy and negative pressure therapy, bio-engineered skin and split-thickness skin graft. Facing the challenges present, Dr Rafik also discussed a case report using negative pressure wound therapy which demonstrated improved healing time.

### Biological and microbiological impact of plasma medicine in wound healing

### Keith Cutting, Clinical Research Consultant, Hertfordshire, UK

The talk was presented by Mr Keith Cutting, clinical research consultant, specialising in tissue viability and related medical devices. Plasma, as a state of matter, is essentially an ionised gas that delivers charged species. Whereas thermal gas plasma is a high temperature plasma (>80 degrees centigrade), which has been used to cauterise, incise and coagulate tissue and to sterilise surgical instruments and implants.

Mr. Cutting's presentation focussed on non-thermal gas plasma (NTGP) and its use as an innovative approach in medicine and specifically in wound care. NTGP operates below body temperature and is non-toxic to mammalian tissue. The plasma is generated inside an ionisation chamber where argon gas is bombarded with electrons. When the plasma comes into contact with air, reactive nitrogen species, reactive oxygen species and UV-light photons are generated. These plasma species have a broad-spectrum antimicrobial impact on tissue, effectively treating Gram positive and Gram-negative bacteria, fungi, viruses and spores. The advantage of NTGP over 'traditional' antibiotic treatment is the avoidance of bacterial selection for resistance. In addition to the antimicrobial action, NTGP stimulates the production of growth factor and cytokine expression. This promotes granulation tissue formation and epithelialisation. NTGP is a contactless therapeutic intervention at a molecular level that can penetrate cavities and fissures down to 9cm.

NTGP has also been found to be effective in a range of dermatological conditions including Hailey-Hailey disease and herpes zoster infection. In the treatment of skin graft donor sites with NTGP significant improvement in healing, when compared to placebo treated areas, have been found. In another study, comparing biofilm treated samples and placebo treated samples a significant increase in bacterial biofilm destruction was also observed. In a current animal study, NTPG demonstrated acceleration of healing and no accumulative effect of reactive oxygen species, thereby avoiding problems of tissue toxicity occurring. An excessive concentration of reactive oxygen species activates pro-apoptotic proteins, and would induce cell death, and in extreme cases cellular necrosis. Treatment is only 3-5 minutes duration per treatment session and improvement in wound healing is generally observed in 1-2 weeks.

At present, widespread knowledge of NTPG is restricted due to its novelty. However, existing evidence has shown great promise of NTGP in both decontaminating acute and chronic wounds and accelerating wound healing, even in genetic conditions associated with poor healing. With more data yet to be published, this therapy proves to offer a well-tolerated, viable and safe treatment.

### Enhanced wound healing with copper oxide impregnated dressings - molecular mechanisms

#### Dr Gadi Borkow, Cupron Inc., Israel

Copper has been used for skin wounds and eye infections since ancient Egypt as well as many other civilisations across history. It has many properties that assist in healing such as having a wide spectrum bactericidal activity, inducing angiogenesis and stimulating the formation of collagen and fibronectin which is essential in skin regeneration. It also creates a zone of inhibition for bacterial proliferation around its application.

Dr Borkow discussed the clinical use of copper oxide included in various polymer materials for wound healing with Cupron socks, which were given to the Chilean miners in 2010 helping to protect their feet from erythema, scaling, fissuring and irritation associated with the humidity, poor hygiene and lack of sunlight from being trapped in the mine. These socks are also used in athlete's foot and diabetic patients with no development of resistance being demonstrated, possibly due to its wide multi-site anti-microbial action.

Dr Borkow also discussed his research of dressings impregnated with copper oxide particles (0.5 - 1 micron in size) for inflicted wounds in genetically engineered diabetic mice [6]. The results demonstrated significant increase in angiogenesis and wound closure with copper oxide dressings compared to controls thus demonstrating enhanced wound healing. Copper impregnated materials have also shown antiviral abilities (for example deactivating HIV-1) as well as potent antibacterial activity, killing even antibiotic resistant bacteria such as methicillin resistant Staphylococcus aureus (MRSA) [7].

The use of copper in dressings shows promising results for clinical application, with no adverse reactions observed such as skin sensitisation and effects gained from copper concentrations well below toxic levels.

### Reactive oxygen and wounds- from the laboratory to the labour ward

### Jonathan Cooke MPharm, PhD, Visiting Professor in the Infectious Diseases and Immunity Section, Department of Medicine, Imperial College London, London, UK

Honey is well-known for its high antimicrobial and wound healing enhancement properties. These assets depend on the chemical and physical components of honey. Professor Cooke presented a number of studies on Surgihoney Reactive Oxygen (SHRO), a sterile bio-engineered honey which generates reacROS are defined as chemically reactive molecules containing oxygen. They have healing properties and are effective even against antimicrobial resistant organisms. ROS are formed as a natural by-product of the normal metabolism of oxygen and have important roles in cell signalling and homeostasis. ROS are involved in each step of the healing process (mediating many actions such as vasoconstriction, neutrophil migration, bacteriostatic action, inducing phagocytosis and triggering cell division and tissue repair). They act as secondary messengers to immunocytes and non-lymphoid cells involved in the wound repair process. ROS participate in the recruitment of lymphoid cells to the wound site to regulate angiogenesis ensuring optimal perfusion and effective tissue repair. Phagocytes induce an ROS burst onto the pathogens present on the wound to destroy them, whilst excess ROS leaks into the surrounding environment to give further bacteriostatic effects. The dilution of SHRO with serum leads to its clinical activity.

tive oxygen species (ROS) when applied to wounds.

SHRO is rapidly active in-vitro against all tested gram positive and gram-negative bacteria as well as having antifungal and antiviral properties. Studies have demonstrated the ability of SHRO to both prevent the formation of and destroy existing biofilms caused by a range of bacteria in cutaneous wounds and respiratory epithelium, thus showing SHRO to be a simple and effective treatment for chronic wounds and clear multidrug resistant organisms, including MRSA, CPE and Escherichia coli from wounds and vascular line sites. This has great potential for the control of the bioburden and biofilm at these sites thus providing an alternative to antibiotics on epithelial/ mucosal surfaces.

Professor Cooke also discussed studies comparing SHRO to different engineered honey, as well as clinical trials assessing wound healing of previously infected wounds and as a prophylactic option. In a before and after study in patients undergoing caesarean section, SHRO demonstrated a 60% reduction in wound infection rates compared to controls. ROS are active from the microbiological scale to the clinical scale, demonstrating significant improvements in the treatment of acute and chronic wounds and long line site infections (such as in burn patients where infection is the major cause of death or cancerous patients), as well as in prophylactic dressings, as an implant coating in complex joint replacement surgery and in chronic urinary tract infections with multi- drug resistant organisms (inserted by cystoscopy).

Compared to other dressings, SHRO presents many of the desired qualities from a dressing: antimicrobial, local wound nutrition, non-toxic, promotes wound healing at a cellular level, wound barrier, moisture control, de-sloughing agent, odour control, pain suppressant.

SHRO is a novel solution to controlling and eradicating bacteria representing a promising avenue for improving wound healing and may also be a key to reducing antibacterial resistance.

### The role of the hair follicle in cutaneous wound healing

Dr M Julie Thornton, Centre for Skin Sciences, Faculty of Life Sciences, University of Bradford, Bradford, UK

Dr Thornton provided insights into the importance of hair follicles in wound healing. Hair follicles, complex tissues composed of discrete populations of mesenchymal and epithelial cells, display striking regenerative properties in the adult. This unique, lifelong cycling is regulated by complex ectodermal– mesenchymal interactions and during wound healing they can provide a reservoir of mesenchymal and epithelial stem cells. Epidermal stem cells are recruited for re-epithelialisation and mesenchymal stem cells for dermal repair. Re-epithelialisation starts around remaining hair follicles and from the marginal epithelium and when the papillary layer is removed, granulation tissue develops at the sites of follicles. When the skin is destroyed to the deep dermis, the regenerating granulation tissue comes from the connective tissue surrounding the hair follicles with scars forming when wounds are deep enough to destroy the hair follicle bulbs. Therefore, the hair follicle is a principal cutaneous structure whose presence or absence conditions the outcome of the healing response. This is reflected clinically in the faster rate of healing seen in hairy skin in wounds and grafts. Interestingly hair follicles also demonstrate the ability to generate and maintain a relatively immune privileged area, which serve to protect the hair follicle stem cells. Another important adnexal structure of human skin are the sweat glands, which are approximately three times more abundant than hair follicles; they are capable of generating keratinocytes, and are the sole appendage assisting in re-epithelialisation of glabrous skin.

Further research towards understanding and utilising these stem cell reservoirs, as well as how hair follicles influence the dermis, may also help in developing skin substitutes and improved therapies for chronic wounds and burns.

### Conclusion

This meeting covered a variety of topics relevant to wound healing, with presentations and posters delivered from different disciplines. Novel research and technologies that were discussed, such as copper, reactive oxygen species and biofilms, provided insights into the status and possibilities of cuttingedge front-line therapies and investigations in wound healing.

### **Meeting Abstracts**

#### Talks

### **Biofilms: A Paradigm Shift in Wound Microbiology**

Professor Steven Percival, 5D Health Protection Group Ltd and University of Liverpool, UK

Understanding the microbiology of chronic wounds requires further intensive research as the majority of studies undertaken to date have relied solely on data generated from agar culture-based technologies. Furthermore, studies have rarely taken into account the more fastidious, slow-growing and unculturable microorganisms. Microorganisms found within a chronic wound environment exist in two phenotypic states, the free floating or planktonic phenotypic state, and the attached or sessile/biofilm phenotypic state. Despite this fact the majority of wound microbiology research has been carried out on microbes residing within the planktonic state. Biofilms are universal in chronic wounds and this virulent state is considered responsible for the recalcitrant nature of chronic wounds and the main reason that an infection occurs.

### Mechanism of wound repair in gastrointestinal tract

### Dr. Narendra Kumar, Associate Professor (Tenured), Department of Pharmaceutical Sciences, TX, USA

Understanding the communication between epithelial cells, immune cells, and microbial population of the gastrointestinal tract has immense implication in understanding the mechanism of various intestinal disorders such as Crohn's disease, ulcerative colitis, and low-grade inflammation mediated metabolic syndrome. Intestinal injury and wound repair plays a central role in the cross-talk between these entity. The talk will highlight the current understanding on the mechanism of gastrointestinal wound repair and their correlation with aforementioned diseases.

### Management of Diabetic Foot Healing: Experience of the National Centre of Burns and Plastic Surgery: Morocco

Amine Rafik\*, Taquafi S, Diouri M, Bahechar N, Chlihi A National Centre of burns and plastic surgery: Morocco

### Introduction

Diabetic foot is a major public health problem by the economic and social cost as of the high rate of amputations it spawns. The purpose of the work is to analyse the clinical and paraclinical factors related to amputations as well as short-term evolution. Materials and methods: Through a retrospective study over 2 years (January 2012-January 2014) dealing with 27 patients supported at the national center of burn and plastic surgery to the CHU Ibn Rochd of Casablanca, having suffered a minor amputation or major injury of the foot. Results: The average age of our patients is 53 years with a net dominance of the male. 70% of patients are patients with type I diabetes. With regard to the degenerative complications, 82% of our patients had neuropathic feet, 25% had a lower limb arteriopathy, and 64.5% of cases are complicated by nephropathy and 16.1% retinopathy. The main factor triggering the foot injury was especially mycotic infection (30%), followed by wounds and burns not felt. Individual lesions are found: phlegmon, evil puncturing Plantar, ischemic ulcer, complicated Erysipelas, and in 25% of cases, the patient consults at the stage of gangrene. Almost half of our patients (54.8%) have suffered major amputation. The evolution was favourable in 45% of the patients and 35% have necessitated a revision surgery. Conclusion: The reduction of the number of amputations through the awareness of practitioners to this problem and the urgency of its support as well as good monitoring and education of diabetes patients.

### Biological and microbiological impact of plasma medicine in wound healing

### Keith Cutting, Clinical Research Consultant, Hertfordshire, UK

Plasmas have been used for a long time in medicine to sterilise medical equipment and implants, and for use in electrosurgery (coagulation). Increasing interest is particularly being shown in the use of non-thermal gas plasma (NTGP) that uses a patented ionisation chamber to emit energised argon gas. NTGP has been shown to be safe, well tolerated and effective; in a range of dermatological conditions, and in acute donor site wounds where it also promotes re-epithelialisation. NTGP has been shown to improve wound healing in vitro and in vivo.

The plasma species delivered to the wound bed includes reactive oxygen and nitrogen species, OH radicals, ions, electrons, and UV light photons that ensure reproducible therapeutic effects. NTGP has bactericidal effect on Gram +ve and Gram –ve microbes, is effective against antibiotic resistant strains, and is antifungal and anti-viral. Anti-biofilm efficacy has been demonstrated in vitro and in an animal model of infected wounds. It is important to note; plasma effect is not temporary and that bacteria do not develop plasma resistance. During plasma treatment no thermal damage is caused, human blood is unaltered, treated human skin histology is unaltered, and there are no morphological changes to HeLa cells.

### Development of novel wound dressings for infection control: exploration of infection-responsive release and prophylactic bacteriophage therapy

### Dr Diana Alves, School of Pharmacy and Biomolecular Sciences, University of Brighton / Blond McIndoe Research Foundation, Brighton UK

Burn wounds are typically colonised by a variety of potential pathogens at sub-clinical levels. This low-level colonisation, not easily detected, progresses to invasive infection, where clinical intervention is required. There is also evidence that infection can influence the healing process and result in increased scarring. However, diagnosis of infection in burn patients is problematic, and often not detected until overt symptoms arise, yet prompt treatment at the earlest onset of infection stands to provide significant treatment and cost benefits. In addition, the range of organisms normally comprising the wound microbiome include those that are often multidrug resistant (MDR), such as Staphylococcus aureus, Pseudomonas aeruginosa and Enterococcus faecalis. We aim to develop infection responsive materials suitable for incorporation in wound dressings, and the delivery of novel antimicrobial agents capable of dealing with key multidrug resistant pathogens. Since we will be targeting MDR organisms, and in light of the current drive to reduce antibiotic usage and identify alternatives, we aim to deliver bacteriophage to the wound bed, which are able to infect and kill target bacteria regardless of antibiotic resistance profile and moreover our results show a clear ability to reduced biofilms caused by those MDR clinical isolates.

### Periodontal wound healing and its enhancement by application of lasers

*Mr Radko Chmurovic, Wise Dental Ltd, Nottingham, UK* Established periodontal wound bears characteristics of chronic and infected lesion. Infective agents form complex biofilms on hard and soft tissues of periodontal pockets and invade its cellular lining. Application of lasers stimulates release of multiple growth factors. Antibacterial photodynamic therapy (aPDT) combines biostimulation of lasers with bactericidal and fungicidal effect of photodynamic reaction. Generated reactive oxygen species are effective against planktonic, sessile and intracellular pathogens. aPDT with certain parameters becomes cytotoxic to human cells. Keratinocytes appear to be more susceptible than other cell lines. Selective ablative effect of aPDT on epithelial lining of periodontal pocket may explain dramatic clinical outcomes.

### Roles of mesenchymal stem cells in cutaneous wound healing

Mr Moyassar Al-Shaibani, Institute of Cellular Medicine, The Faculty of Medical Sciences, Ground Floor William Leech Building, Newcastle University, Framlington, Newcastle upon Tyne, UK

Mesenchymal stem cells (MSCs) and their secretions have gained attention as promising tools to promote wound healing. Two main strategies could be applied for the use of MSCs in the treatment of non-healing wounds. MSCs show ability to differentiate into the different cells of skin epidermis. Also, MSC secretions collected from in vitro cultures, which are known as MSC-conditioned medium (MSC-CM), are reported to promote migration of skin cells such as keratinocytes and fibroblasts into the injury site. Also, MSC-CM enhances the differentiation of primary keratinocytes into the different layers of epidermis.

### **Results of the interim analysis of the SAWHI-V.A.C.-study** *D Seidel, C Könen, R Lefering, E Neugebauer*

Background: A decision of the Federal Joint Committee Germany states that negative pressure wound therapy is not accepted as a standard therapy with full reimbursement by health insurance companies in Germany. This decision is based on the reports of the Institute for Quality and Efficiency in Health Care, which demonstrated that an insufficient state of evidence regarding the use of negative pressure wound therapy (NPWT) for acute and chronic wounds exists. The aim of the SAWHI-V.A.C.®-study is to compare the clinical, safety and economic results of both treatment arms and to generate solid evidence regarding the effectiveness of NPWT. Methods: The independent scientific Institute for Research in Operative Medicine as part of the University of Witten/Herdecke initiated a randomised controlled clinical trial to evaluate the effectiveness and safety of NPWT for the treatment of subcutaneous abdominal wound healing impairment after surgery compared with standard conventional wound therapy. The trial is financed and supported by the manufacturer Kinetic Concepts Incorporated (KCI / Acelity). After including 278 patients one planned interim analysis was performed to evaluate if there is a significant positive or negative effect for V.A.C.®-therapy and the trial should be stopped. Results: Starting in August 2010 this multinational clinical trial showed despite all obstacles that the performance of randomised controlled clinical trials in wound healing is possible. In October 2014 the number of patients for the planned interim anylysis was reached. At the timepoint of the interim analysis no superiority of one treatment arm was demonstrated for the primary endpoint time (number of days) to achieve complete, sustained and photo-verified wound closure. For the secondary endpoint wound closure rate the number of confirmed wound closures was higher in the V.A.C.® treatment group than in the standard conventional wound treatment group. Conclusion: The recruitment continues. The final analysis of the trial will be performed after reaching the a priori calculated overall sample size of 550 patients to be analysed. Overall study results will be provided to contribute to the final decision of the Federal Joint Committee Germany regarding the general admission of negative pressure wound therapy as a standard performance within both medical sectors in Germany.

## Sub-molecular aspect of tyrosine kinase mediated mucosal wound repair

### Jayshree Mishra, Narendra Kumar

Department of Pharmaceutical Sciences, Irma Lerma Rangel (ILR) College of Pharmacy, Texas A&M Health Science Center, Kingsville, Texas 78363, USA.

### Introduction

Inflammatory bowel disease is characterised by a chronic inflammation of the intestinal mucosa. The mucosal epithelium of the gastrointestinal tract constitutes a key element of the mucosal barrier to a broad spectrum of deleterious substances present within the intestinal lumen including bacterial microorganisms, various dietary factors, gastrointestinal secretory products and drugs. Epithelial cells in the gastrointestinal mucosa play an important role in defining the physical barrier between the host and the external environment. This protection by intestinal epithelial cells is maintained by a highly dynamic and continuous cross-talk between the intestinal epithelial cells and the immune cells of the gas-trointestinal tract. Previously, we demonstrate that intestinal epithelial cells express function-

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ally specific Jak3, a potent non-receptor tyrosine kinase and regulates IL 2 induced mucosal would repair through tyrosine phosphorylation of an actin binding protein villin thereby facilitating cytoskeletal remodelling and wound repair. Here we determined the structural determinants that regulate the interactions between Jak3 and villin that has important implications in transplant biology, epithelial wound repair, cancer metastasis, and immune cell migration. Method: Wild type or mutant Jak3 cDNAs cloned in pGEX-4T or p6X His-ET were expressed in Escherichia coli BL21 or TKX1 cells to get the non-phosphorylated and phosphorylated form of the Jak3 protein. In vitro kinase and pairwise binding assays were developed and kinetic parameters were determined. PCDNA-HA-Jak3-wt and pCD-NA-HA-Jak3-V484\* were stably transfected into the HT-29 CL19 A cells to determine the importance of Jak3 function in cell culture model. Results: Recombinant Jak3 autophosphorylates itself and transphosphorylates the cytoskeletal Protein villin. P-Jak3-wt interacted with P-villin-wt in a dose-dependent manner with a Kd of 23 nm and a Hill's coefficient of 3.7. FERM Domain of Jak3 was found to be sufficient for the Interactions between Jak3 and Villin. Tyrosine Phosphorylation of Jak3-SH2 domain facilitated the interactions between villin and Jak3. Intramolecular Interactions between FERM and SH2 Domains of Jak3 prevented Jak3 Interactions with villin. Conclusion: Tyrosine phosphorylation of SH2 domain of Jak3 facilitated the interactions between the Jak3-FERM domain and cytoskeletal proteins and understanding of Jak3 functions has important implications in epithelial mucosal wound repair.

### Enhanced wound healing with copper oxide impregnated dressings - molecular mechanisms

### Dr Gadi Borkow, Cupron Inc., Israel

Copper plays a key role in angiogenesis and skin regeneration. We demonstrate that application of wound dressings containing copper oxide to wounds inflicted in genetically engineered diabetic mice resulted in increased gene and in-situ upregulation of pro-angiogenic factors (e.g., PLGF, HIF-1a and VEGF), increased blood vessel formation (p<0.05) and enhancement of wound closure (p<0.01) as compared to control dressings (without copper) or commercial wound dressings containing silver. In diabetic patients, who responded poorly to conventional wound healing treatments, their application resulted in wound closure. We will discuss the molecular mechanism by which copper oxide impregnated dressings stimulate wound healing.

### Reactive oxygen and wounds- from the laboratory to the labour ward

### Jonathan Cooke MPharm, PhD, Visiting Professor in the Infectious Diseases and Immunity Section, Department of Medicine, Imperial College London, London, UK

Reactive Oxygen (RO) is a novel solution to controlling and eradicating bacteria. RO is rapidly active in-vitro against all Gram positive and Gram negative bacteria tested. RO also has some antifungal and antiviral properties. In addition, studies have demonstrated the ability of RO to prevent the formation of biofilms caused by a range of bacterial species in wounds and in respiratory epithelium. RO has been shown to be a simple and effective treatment for chronic wounds and clears multi-drug resistant organisms, including MRSA, and CPE Escherichia coli from wounds and vascular line sites. This has great potential for the control of bioburden and biofilm at these sites, thus providing an alternative to antibiotics on epithelial/ mucosal surfaces. A controlled before and after study in patients undergoing Caesarean Section, RO demonstrated a 60% reduction in wound infection rates.

### Extracellular PKM2 facilitates wound healing by promoting myofibroblast differentiation and angiogenesis

Dr Zhi-Ren Liu, Georgia State University, USA

We report here that the activated neutrophils at the wound site release PKM2, a glycolytic enzyme, by its secretive mechanisms during early stages of wound repair. The extracellular PKM2 facilitates wound healing by promoting early granulation and angiogenesis. PKM2 facilitates formation of early granulates by promoting fibroblast migration and myofibroblast differentiation. We demonstrated that extracellular PKM2 promotes myofibroblast differentiation by a TGFb independent pathway via activation of integrin avb3 signaling. Our studies reveal a new molecular linker between the early inflammation response and proliferation phase in wound healing process. Our studies also uncover a novel mechanism of promoting myofibroblast differentiation.

### The role of the hair follicle in cutaneous wound healing

Dr M Julie Thornton, Centre for Skin Sciences, Faculty of Life Sciences, University of Bradford, Bradford, UK

Hair follicles are found in human skin with few exceptions. Discrete populations of mesenchymal and epithelial cells, they have striking regenerative properties, cycling throughout adult life recapitulating events of embryogenesis. During wound healing their reservoir of epidermal stem cells are recruited for re-epithelialisation and mesenchymal cells for dermal repair. A greater understanding of the wound healing properties of hair follicle epithelial and mesenchymal subpopulations, together with an understanding of how the type of hair follicle may influence the dermal environment, may help in the development of skin substitutes for the treatment of chronic wounds and major burns.

### Analysis of Polymicrobial Biofilm Infections in Non-Healing Diabetic Ulcer

### Karthika S1, Joby John2 and Sabu Thomas1,\*

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Chronic diabetic ulcer is one of the major devastating complications of diabetes and precedes 84% of all diabetes-related lower-leg amputations. Such chronic infections are associated with bacterial burden which exist as biofilm communities. The biofilm phenotype infections which are highly resistant to antibiotics and host immune response are considered as primary hindrance to the healing of chronic wounds. In the present investigation, swabs and debridement samples were collected from chronic diabetic ulcer patients to study the nature and composition of bacteria in the wound infections. The bacterial diversity analysis by 16S rRNA gene sequencing revealed that Pseudomonas aeruginosa (40%), Proteus spp. (32%), Enterococcus spp. (30%) and Staphylococcus spp. (25%) are the predominant genera associated with the wound infections. Majority of the infections are polymicrobial in nature and 25 bacterial genera are consistently identified. Antibiotic profiling of these bacterial isolates unveiled that majority of them are multi-drug resistant which showed resistance to Penicillins, Fluorquinolones, Cephalosporins and even glycopeptides. Biofilm assay revealed that all the Proteus isolates (100%), Enterococcus isolates (96%), Pseudomonas isolates (91%) and Staphylococcus isolates (81%) are strong biofilm producers. The biofilm architecture and its thickness are evaluated by Confocal Laser Scanning Microscopy (CLSM) using LIVE/ DEAD BacLight<sup>TM</sup> Bacterial Viability Kit. The occurrence and establishment of bacterial biofilm over chronic wound tissues is proved via Fluorescent in situ Hybridisation (FISH) using 16SrRNA universal probes. The Scanning Electron Microscopy imaging also demonstrated the presence of biofilm aggregates over chronic wounds. The present study gives a clear picture of chronic wound pathogenic biofilms that inturn explains why chronic wounds does not heal despite adequate antibiotic treatment and it gives us new paths of research that may lead to new treatment strategies using biofilm inhibition.

# The role of the fibroblasts and TGF- $\beta$ (transforming growth factor beta) on the wound healing: hypertrofic and keloid scars

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### Abstract

Backgroud: Understanding the normal sequence of wound healing is important before knowing the pathophysiology and treatment of keloids and hypertrophic scars. Individuals of all ethnic backgrounds can form keloid and hypertrophic scars as a familial predisposition was believed no exist. There are no clearly defined genetic loci conferring risk for keloids. Factors that are responsible for this are: Inflammation, fibrogenic response, genetics and hormonal factors. The fibrogenic response is the central to the formation of hypertrophic and keloid scar tissue is an alteration of the fibroblast phenotype. Indeed, when compared with normal fibroblasts, keloid fibroblasts show increase numbers of growth factor receptors and response more briskly to growth factor like TGF-B (Transforming Growth Factor beta), which may upregulate these abnormal cells from the beginning of wound healing. Recent studies indicate that TGF-B play an integral role in the formation of keloids. TGF-\u00b31, TGF-\u00b32 and TGF-\u00b33, are three isoforms that exists. TGF- $\beta$ 1 is thought to be profibrotic, whereas, TGF-β3 may have anti-fibrotic functions. The overproduction of the subtype TGF- $\beta$ 1 is associated with an excessive deposition of scar tissue and fibrosis. TGF- $\beta$  modulates the expression of matrix metalloproteinase (MMPs) which is capable all

the components of the extra cellular matrix and the basement membrane.

Objectives: To do a literature revision and update focused in the role of the fibroblasts and FGF-  $\beta$ , on the pathogenesis and molecular mechanisms, in the Hypertrophic and keloid scars healing wound. To provide at physicians can better understand and properly treat such lesions. Methods: A medicine literature search was performed for relevant publications and for diverse strategies for management of hypertrophic scars and keloids. **Conclusions:** Elucidation of the molecular pathways leading to keloid formation will undoubtedly open up a host of opportunities. Recent studies indicate that TGF- $\beta$  (Transforming Growth Factor beta) play an integral role in the formation of keloids. In the future, development of selective inhibitors of TGF-β might produce new therapeutic tools with enhance efficacy and specificity for the treatment of keloids. The authors have indicated no significant interest with commercial supporters

### Posters

### Analysis of Polymicrobial Biofilm Infections in Non-Healing Diabetic Ulcer

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Chronic diabetic ulcer is one of the major devastating complications of diabetes and precedes 84% of all diabetes-related lower-leg amputations. Such chronic infections are associated with bacterial burden which exist as biofilm communities. The biofilm phenotype infections which are highly resistant to antibiotics and host immune response are considered as primary hindrance to the healing of chronic wounds. In the present investigation, swabs and debridement samples were collected from chronic diabetic ulcer patients to study the nature and composition of bacteria in the wound infections. The bacterial diversity analysis by 16S rRNA gene sequencing revealed that Pseudomonas aeruginosa (40%), Proteus spp. (32%), Enterococcus spp. (30%) and Staphylococcus spp. (25%) are the predominant genera associated with the wound infections. Majority of the infections are polymicrobial in nature and 25 bacterial genera are consistently identified. Antibiotic profiling of these bacterial isolates unveiled that majority of them are multi-drug resistant which showed resistance to Penicillins, Fluorquinolones, Cephalosporins and even glycopeptides. Biofilm assay revealed that all the Proteus isolates (100%), Enterococcus isolates (96%), Pseudomonas isolates (91%) and Staphylococcus isolates (81%) are strong biofilm producers. The biofilm architecture and its thickness are evaluated by Confocal Laser Scanning Microscopy (CLSM) using LIVE/ DEAD BacLight<sup>™</sup> Bacterial Viability Kit. The occurrence and establishment of bacterial biofilm over chronic wound tissues is proved via Fluorescent in situ Hybridisation (FISH) using 16SrRNA universal probes. The Scanning Electron Microscopy imaging also demonstrated the presence of biofilm aggregates over chronic wounds. The present study gives a clear picture of chronic wound

pathogenic biofilms that inturn explains why chronic wounds does not heal despite adequate antibiotic treatment and it gives us new paths of research that may lead to new treatment strategies using biofilm inhibition.

### Efficacy of Fibrin Rich in Platelets (L - Prf) On Wound Healing

Amine Rafik\*, Jouhri K, Diouri M, Bahechar N, Chlihi A National Centre of burns and plastic surgery: Morocco

### Introduction

Concentrate autologous platelets (PRP and L - PRF) are widely studied as a means of speeding up the healing without evidence of their effectiveness. Dental surgery clinical outcomes are very encouraging, but at the moment, there is no prospective, randomised study that evaluates their effectiveness on the healing of the skin. This clinical randomised controlled study evaluated the effectiveness of one of these concentrates, (L -PRF) platelet-rich fibrin, on skin healing

### **Materials and Methods**

A National center of burns and plastic surgery in Morocco, included patients were randomised in two groups, the group where the wound was covered with wireless and the control group where the wound was covered with fatty dressing according to the usual technique. The patients were followed for 2 months after their intervention with systematic photograph taken

### Results

48 patients were included and randomised in the study (Group L - PRF 23 and 25-controlled group). The median time of healing for the Group L - PRF was 22 days (IQR 18-24) and for the Group control was 29 days (IQR 22-36) with a statistically significant difference. Bleeding, exudate and postoperative pain were always lower in L - PRF but without significant difference.

### Conclusion

This study opens up interesting lines of research since the application of L - PRF can accelerate the healing of the surgical wound in a meaningful way with median improvement of 5 days.

### Adipose-Derived Stem Cells: Characterisation and Potential for Wound Healing

Amine Rafik\*, Samira Taquafi, Naima Bahechar, Abdessamad Chlihi

### Introduction

The use of stem cells from adipose tissue or Adipose Derived Stem Cells (ASC) in regenerative medicine appears as an attractive alternative to cell strains of bone marrow because they are present in large quantities and obtained more easily. Human adipose derived mesenchymal stem cells are thought to be potential key factors for starting the regenerative process after tissue injury.

### **Material and Methods**

In the National center of burns and plastic surgery, CHU Ibn-Rochd Casablanca, Morocco. A retrospective review of all patients admitted during 2011–2014, who developed Ulcer of the leg and was treated by lipofilling. Patient demographic data and digital photographs were taken on the day of surgery and every other day thereafter. Time to wound closure was defined as the time at which the wound bed was completely reepithelialized and filled with new tissue.

### Results

These patients had mean age of 24.3 years. Measurement of the healing time shows the effectiveness of the ASC of adipose on healing time as complete the closure wound obtained after 3 sessions of injection of 20cc ASC. Our results revealed that the average time for wound closure in the ASCs group was  $13 \pm 0.87$  days whereas the time in the control group was  $19 \pm 0.61$  days. Clinical applications of ASCs have begun to show early safety results and promising possibility of efficacy in patients with a range of diseases, including peripheral vascular disease, bony tissue defects. and skin wounds. These effects are importantly based on the secretion of trophic and survival factors by these cells and by their participations in the growth and remodeling of blood vessels.

### Conclusion

In conclusion, this study presented that accelerated wound healing could be achieved by local transplantation of autologous ASCs. Moreover, some clinical aspects of wound healing as well as the possibility of the therapy based on stem cells might represent a feasible therapeutic approach in treatment of clinical wounds.

### The Chronic Wound: Aspect Clinical and Evolutive Amine Rafik\*, Chabbak H, Diouri M, Bahechare N, Chlihi A

National Centre of burn and plastic surgery Casablanca, Morocco

### Introduction

Marjolin's ulcer is malignant degeneration of an inflammatory injury chronic. However, this term is often correlated with cancers occurring on burn scars because the unstable scar constituting the form conducive to the development of skin cancer.

### **Materials and Methods**

The objective of our work is to describe the characters epidemiologic, therapeutic and prognostic of this pathology through the study of a series of 20 cases collected at the national center of burn and reconstructive surgery CHU IBN ROCHD CASA-BLANCA from 2010 to 2015 with review of the literature.

### Results

The average age of our patients is 54 years with male-dominated, these lesions most often grafted on initial Burns: deep and little extended having been left in spontaneous healing or received inadequate treatment with inadequate follow-up which will take the appearance of tumors Ulcer-burgeoning degenerative infected. In order of frequency were individualised 3 cases of axillary localisation and the upper limb; 14 cases involving leg and the popliteal fossa. The time of onset ranged between ten and fifteen years in our patients. The positive diagnosis is based on biopsies - wide resection with pathological studies confirming ballistics malignancy having objectified through our series of squamous cell carcinomas with affected lymph node positive in more than 75% of cases with in other cases of Melanoma lesions or sarcoma. Our surgical treatment appealed to broad oncological resections with routine lymphadenectomy while means of coverage will be tattered initial mobilisations

in 16 cases of flaps scapulars or fascio-cutaneous leg; skin graft with a last recourse to amputation in two cases. The prognosis is reserved with the possibility of recurrence or metastases.

### Conclusion

Skin cancers on scar burning remains a rare and increasingly observed complication in fasting treatment whatever aggressive must be early and well coded.

### Burns Wound Healing; Epidemiology and Clinical Features

#### Kawtar Johri, Amine Rafik, Michraf FZ, Samira Taquafi, Naima Bahechar, Mounia Diouri, Abdessamad Chlihi

National Center for Burns and Plastic Surgery, CHU IbnRochd, Casablanca, Morocco

### Introduction

The diluent; chemical liquid (refined petroleum distillate containing aliphatic and aromatic hydrocarbons) normally used to dilute an already more or less liquid substance is a not uncommon cause of burns in our Moroccan context.

### **MATERIAL AND METHODE:**

This work is a retrospective study over a period of 1 year (January 2015 - January 2015) who helped collect 18 cases of thermal burn flame by diluting a total of 400 cases of patients admitted for burns distinct agents. The average age of these patients is 30 years. They are almost all male low socioeconomic status and history of substance abuse and / or delinquency.

### Result

The burn is often secondary to an assault in the street (90% of cases) or accidental in the context of drug abuse (8% of cases) or psychosis (2% of cases). Regarding the characteristics of the burn, the average burned skin surface is 25%; it is often profound requiring skin grafting in all our patients in this series and especially seat at the front of the trunk and upper limbs. The lung damage if inhaled concerned 30% of patients in our series.

The thinner flames burn is a severe burn both general plans saw the risk of respiratory injury (acute respiratory distress, lesional pulmonary edema, pulmonary infection ...) on the local state; these being immediately deep burns are responsible for significant aesthetic and functional sequelae.

### Conclusion

Preventing these burns through the regulation and control of the sale of the product and information about its dangers.

### **Clinical Efficacy of the 830nm Led Phototherapy for Burn Patients**

### BJ Rhee, JU Yu, JH Ko

College of Medicine, Hallym University, Hangang Sacred Heart Hospital, Seoul, Korea

**Purpose:** Phototherapy uses the changes caused by the athermal and atraumatic absorption of the photon's energy by the tissue for therapeutic effect. Phototherapy has been proven to be useful in various conditions, for example, in pain attenuation, wound healing and skin rejuvenation. The aim of this research was to evaluate the clinical efficacy of 830 nm LED phototherapy for burn patients.

**Methods:** We recruited 11 patients who visited this hospital between June and December 2012 with superficial 2nd degree

burns to the face for comparative analysis. For phototherapy, we used infrared LED with wavelength of 830 nm. For comparative analysis, we covered one side of the face with sterile aluminum foil and fabric during the treatment. Photographs were taken at the time of each treatment and the time taken for epithelialisation and the level of patient satisfaction were also investigated.

**Results:** All 11 patients were male and the mean age was 44.0  $\pm$  11.9 years (range of 28-63 years). The cause of the burns was flame burn for 7 patients, and electric sparks in 4 patients. The time taken to achieve epithelialisation after the burns was 8.1  $\pm$  2.2 days (range 4-12 days) for the side that received photo-therapy, while it was 9.1  $\pm$  2.9 days (range 4-14 days) for the side that was not treated with phototherapy. In terms of patient satisfaction, 3 patients were 'Very Satisfied', 6 patients were 'Satisfied', 2 patients replied 'Adequate' and none of the patients were 'Unsatisfied'.

**Conclusion:** LED phototherapy of 830 nm wavelength can shorten the time taken for burn wound healing. It also was not associated with serious complications except for skin dryness, so it can be a useful treatment method for burns that produces satisfactory outcome for the patients.

### Burn Wound Dressings- A Review of Peptide Hydrogel Dressings

### Dhaliwal K, Lopez N, Aude Perusseau-Lambert

Division of Surgery and Interventional Science, University College London, Royal Free NHS Foundation Trust, NW3 2QG.

'One of the greatest medical needs is an ideal replacement or means of regenerating damaged skin.' (Larry Hench)

Wound healing is a global medical concern, in particular burns wound healing. Burns are among the leading causes of disability and, annually, 27 million burns occur that require professional treatment, and of these, 7 million require hospitalisation. Currently there is no universally accepted gold standard of burns dressing, however hydrogels dressings are widely used in the clinical setting. Hydrogels are a three-dimensional networks of polymer chains that are water insoluble. They can be made from a number of different natural or synthetic materials. Peptide hydrogels are a type of natural hydrogel that have been successfully demonstrated to aid wound healing. These materials have an innate tendency to self- assemble into biomimetic scaffolds and have shown promise in clinical applications. The regenerative properties of these materials have been further enhanced by incorporation of bioactive agents such as growth factors.

We present a review of the use of peptides hydrogels in wound dressings, with a particular focus on novel short and ultrashort peptides. We discuss the properties of these materials and their successful clinical application in burns wound healing.

### Skin Tissue Regeneration – The Role Bioengineering and its Application in Reconstructive Surgery Dhaliwal K, Dosanjh P

Division of Surgery and Interventional Science, University College London, Royal Free NHS Foundation Trust, NW3 2QG.

Bioengineering plays an essential role in plastic and reconstructive surgery. Recent advances in material science, tissue engineering and stem cell research have enabled the development of novel materials that assist in restoring the body's natural healing capacity. Traditionally the gold standard of skin replacement is an autograft; however, over time, the shortage of suitable, natural tissue for reconstructive and plastic surgery has led to the bioengineering of a number of artificial skin substitutes. The focus is now on developing biomaterials that interact synergistically with their surroundings and promote the body's own regenerative capacities. Skin substitutes have been developed, overtime, from early inert materials to advanced bioengineered, biologically active materials that are able to actively respond to the host and release a number of factors to aid wound healing. The successful use of artificial skin has had a positive impact on burn surgery and the treatment of chronic wounds. We present a review of the development of bioengineering and the application of engineered skin constructs in burns and chronic wounds.

### Modulation Induced by a New Thiazolidine Compound (Gq-11) In Wound Healing on Type 2 Diabetes Animal Model

### Silva JC, Koh T, Mirza R, Bonini M, Abdalla DSP

\***Corresponding author:** Silva JC, Avenida Professor Lineu Prestes, 580 - Bloco 17 - Laboratório de Bioquímica Clínica -Cidade Universitária - CEP 05508-000 - São Paulo/SP – Brasil

**Introduction:** Thiazolidinediones (TZDs) comprise a class of hypoglycemic drugs which reduce insulin resistance in peripheral tissues, mediated by peroxisome proliferator-activated receptors (PPARs) activation. Recently, these drugs have been associated to important side effects, increasing the search for new thiazolidine compounds, which could share beneficial effects and minimise side effects were propelled.

AIMS: These studies aimed to observe wound healing modulation by a new thiazolidine compound - GQ-11 - treatment.

**Methods:** MKR and FVB mice were anesthetised and subjected to excisional wounding with an 8 mm biopsy punch. Healthy tissue collected was stored to use as individual control. Topic treatment was initiated 3 days postinjury, by the groups: GQ-11 – new thiazolidine compound (2mM) and F-127 pluronic gel (vehicle) for 4 days. Wounds extracted were analysed by histology and qRT-PCR.

**Results/Conclusion:** Our data showed that GQ-11 modulates cytokines with important role in inflammation processes. It was possible to observe modulation on M1 macrophages phenotype to M2 macrophages by topical treatment, balancing pro- and anti-inflammatory phases in wound healing inflammatory stage, downregulating TNF $\alpha$  and upregulating ARG-1 and IL-10, leading to tissue repair improvement and cell organisation in diabetic mice. These results turn GQ-11 into a promising alternative on healing/ tissue repair therapy and treatment.

### Expression of Antibacterial Wound Healing Agent Lucifensin of Lucilia Sericata at Different Life Stages Gürgel A, Ozkan B, Yürük M, Yazar S, Kuk S

### *Erciyes University, Medical Faculty, Department of Parasitology, Kayseri-Turkey*

Lucilia sericata adult's colors are metallic green or bluish-green and 5-10mm in size. The most important medically feature of these flies is used maggot debridement treating. Egg, larvae, pupa and adult stages are available in life cycle of L. sericata. There are three main features of the larvae: to debride necrotic tissue, wound and provide disinfection and sterilisation to stimulate wound healing. Life stage, especially the many molecules that are secreted from the larval stage is had function at maggot debridement therapy. Important compounds lucifensin, which have recently been identified in the medicinal larvae of the blowflies L. sericata. The immunomodulator functions and bactericidal role of lucifensin secreted into the infected wound by larvae during Maggot debridement treatment was known.

In this study, the level of lucifensin expression was investigate obtain from the eggs, larvae, pupa and adults of the L.sericata provided the continuity. Total RNA Isolation was made from larvae and synthesised cDNA of these total RNA was used for Real-Time PCR. The level of Lucifensin expression is low at egg stage while larvae, pupa and adult stages of Lucilia sericata were found to have high levels as ,32,31,28 Cp, respectively. acccording to data, we found the most increasing expression of lucifensin gene at adult stages.

Further studies will be done with lucifensin in wound healing could contribute to new perspectives.

### Expression of Lucimycine: A Novel Antifungal Wound Healing Agent at Life Stages of Lucilica Sericata Karaca S, Ozkan B, Yürük M, Gürgel A, Yazar S, Kuk S

Erciyes University, Medical Faculty, Department of Parasitology, Kayseri-Turkey

Lucilia sericata has been used for wound healing recently. Lucilia sericata which are used as therapeutic adult's colors are metallic bluish-green or green and about 10mm size. The most important medically feature of Lucilia sericata is to use for maggot debridement treating. Egg, larvae, pupa and adult stages are available in life cycle of L. sericata. Larvae are used for the Maggot debridement treatment. There are three main features of the larvae: to wound healing, debride necrotic tissue and provide sterilisation and disinfection to stimulate wound healing. Life stage, especially the many molecules that are secreted from the larval stage is had function at maggot debridement therapy. One of the most important compounds lucimycin, which have recently been identified in the medicinal larvae of the blowflies L. sericata. The immunomodulator functions and anovel antifungal protein which composed 77 amino acid roles of lucimycin secreted into the infected wound by larvae during Maggot debridement treatment was known. Lucimycin is active againist fungus.

In this study, the level of lucimycin expression was investigate obtain from egg, larvae, pupa and adult stages L.sericata. Total RNA Isolation was made from larvae and synthesised cDNA of these total RNA was used for Real-Time PCR.

### Expression of Lucimycine is the Highest Level at Third Stage Larva, Pupa and Egg are Stable and Decreasing Along Adult Stage

Further studies will be done with lucimycin in wound healing could contribute to new perspectives.

Reconstructive Options on Traumatic Facial İnjuries Uçak M<sup>1</sup>, Ozkan B<sup>2</sup>

<sup>1</sup>Nevsehir state hospital Departmen of plastic Surgery/ TUR-KEY

<sup>2</sup>Erciyes Universty Department of Medical Parasitology Kayseri/TURKEY

The most cause of facial tissue defect is due to traffic accident. On the other hand, the gunshut wounds and burn injuries are commonly observed becasue of the war in Syria. Several different reconstrictive technique are exist to repair these types defects. In this case report the injury on the facial region was extensively wide which cannot be repaired by routine reconstrictive method.

#### ijclinmedcasereports.com

In our case, 9-year-old girl had an approximately 40x30 cm broad tissue defect on left temporal region comprising the servical region after injuried by gun fire during the war in Syria. And also, the temporal bone was seen by eyes. The bone defect on the left temporal region was repaired by the pectoralis major myocutaneaus flap. The remained other wide tissue defect was repaired by STSG skin greft obtained from left femoral region. In conclusion, the wound size and its location on the facial area limit the reconsctrictive approaches. This kind of cases who have wide tissue defects normaly do not survive or have greft failure and infection on the greft side. Normally, the esthetic concern was ignored during the reconstrictive approach to this kind of wide defects. In this case, we aimed to repair the defect area to obtain a best result in terms of functionality.

### The Nature of Beta-Glucans- and the Role in Wound Care of a Novel Bioactive Beta-Glucan Gel – Woulgan Cutting KF

#### Briery Field, Chorleywood, Herts, UK

Aim: To explore the natural polymer Beta-Glucan ( $\beta$ -glucan) and how a novel bioactive Class III product 'Woulgan Bioactive Beta-Glucan Gel' offers a revolutionary new approach in the management of dry and low to moderately exuding dermal wounds.

**Method:** Literature search was undertaken using PubMed database to retrieve articles related to the; technical profile of  $\beta$ -glucan, mode of action, general relevance to healthcare and specific relevance to wound care.

Results / discussion: β-glucans comprise a group of natural polymers typically found in the cell walls of yeasts, fungi and bacteria, but also in algae and grain. They have wide applications in healthcare including cancer, diabetes, hypercholesterolemia, metabolic syndrome and have a marked capacity to modulate the immune system. Central to the immuno-modulatory capability of  $\beta$ -glucan is the activation and recruitment of macrophages. Macrophages are important wound cleansers and debride the wound of devitalised tissue and dead neutrophils. Macrophages also express a range of growth factors and thereby support cellular proliferation, angiogenesis, deposition of ECM, promotion of re-epithelialisation, and increase in wound tensile strength. Woulgan, containing 2% soluble beta-glucan from yeast, is intended for use on dry, low to moderately exuding wounds that failed to progress under standard care within the preceding 4 weeks.

**Conclusion:** Woulgan Bioactive Beta-Glucan gel is a natural but technologically advanced polymer gel that has been prepared as a primary dressing for stalled wounds. Its immune modulating capability recruits macrophages to the wound bed where the resulting biochemical and cellular responses deliver an accelerated rate of wound closure.

#### Soy Protein Based Hydrogels for Wound Healing Tansaz S, Durmann AK, Detsch R, Schulte M, Harhaus L

#### and Boccaccini AR

*Institute of Biomaterials, University of Erlangen-Nuremberg, Cauerstr.*6, 91058 Erlangen, Germany

Hydrogels are interesting soft based materials for wound healing applications owing to create moist environment by high water content. In this study, plant derived soy protein isolate which has less immunogenicity and proper degradability in comparison to animal derived proteins combined with naturally alginate hydrogel which has a long history in wound dressing applications. We hypothesised that soy protein can promote wound healing by its phytoestrogens. Moreover, for the angiogenesis properties the nano sized bioglasses were added to these hydrogels. The cell-material interaction in 2D was assessed by seeding mouse embryotic fibroblasts and human adult low calcium high temperature keratinocytes on alginate and alginate/soy protein isolate hydrogel films.

### **Reconstructive Options on Traumatic Facial Injuries** Uçak M<sup>1</sup>, Ozkan B<sup>2</sup>

<sup>1</sup>Nevsehir state hospital Departmen of plastic Surgery, Turkey <sup>2</sup>Erciyes University Department of Medical Parasitology Kayseri, Turkey

#### Abstract

The most cause of facial tissue defect is due to traffic accident. On the other hand, the gunshot wounds and burn injuries are commonly observed because of the war in Syria. Several different reconstructive techniques are existing to repair these types defects. In this case report the injury on the facial region was extensively wide which cannot be repaired by routine reconstructive method.

In our case, 9-year-old girl had an approximately 40x30 cm broad tissue defect on left temporal region comprising the servical region after injured by gun fire during the war in Syria. And also, the temporal bone was seen by eyes. The bone defect on the left temporal region was repaired by the pectoralis major myocutaneaus flap. The remained other wide tissue defect was repaired by STSG skin greft obtained from left femoral region. In conclusion, the wound size and its location on the facial area limit the reconstructive approaches. This kind of cases who have wide tissue defects normally do not survive or have greft failure and infection on the greft side. Normally, the esthetic concern was ignored during the reconstructive approach to this kind of wide defects. In this case, we aimed to repair the defect area to obtain a best result in terms of functionality.

### References

- Percival SL, McCarty SM, Lipsky B. Biofilms and Wounds: An Overview of the Evidence. Advances in Wound Care. 2015; 4(7): 373-381.
- Mishra J, Kumar N. Adapter Protein Shc Regulates Janus Kinase 3 Phosphorylation. Journal of Biological Chemistry. 2014; 289(23): 15951-15956.
- Mishra J, Verma RK, Alpini G, Meng FY, Kumar N. Role of Janus Kinase 3 in Mucosal Differentiation and Predisposition to Colitis. Journal of Biological Chemistry. 2013; 288(44): 31795-31806.
- Mishra J, Karanki SS, Kumar N. Identification of Molecular Switch Regulating Interactions of Janus Kinase 3 with Cytoskeletal Proteins. Journal of Biological Chemistry. 2012; 287(49): 41386-41391.
- Mishra J, Verma RK, Alpini G, Meng FY, Kumar N. Role of Janus Kinase 3 in Predisposition to Obesity-associated Metabolic Syndrome. Journal of Biological Chemistry. 2015; 290(49): 29301-29312.
- Borkow G, Gabbay J, Dardik R, Eidelman AI, Lavie Y, Grunfeld Y, et al. Molecular mechanisms of enhanced wound healing by copper oxide-impregnated dressings. Wound Repair and Regeneration. 2010; 18(2): 266-275.
- Borkow G, Gabbay J. Putting copper into action: copper-impregnated products with potent biocidal activities. Faseb Journal. 2004; 18(12): 1728-+.