DBM FACTS

Periodisches Informationsblatt des Departementes Biomedizin
Universität Basel, Universitätsspital Basel und
Universitäts-Kinderspital beider Basel

Geburtshilflicher Alltag in Tansania | It's Christmas in Accra | Silvester in unterschiedlichen Ländern

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IMPRESSUM

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EDITORIAL

Radek Skoda
Leiter DBM

Liebe Leserinnen und Leser

Für die meisten von uns ist der Jahreswechsel Anlass, das vergangene Jahr Revue passieren zu lassen. Von mancher Seite habe ich im zu Ende gehenden Jahr «Glückliches DBM» gehört und ich wünsche uns allen, dass es noch lange so bleibt. Aber wir müssen auch vorwärts schauen: Es gibt in den kommenden Jahren viele wissenschaftliche, strategische und organisatorische Herausforderungen zu meistern. Der Erfolg ist wesentlich von den Menschen abhängig, die am DBM tätig sind und die das DBM erst ausmachen. Nehmen wir den anderen und seine Arbeit wahr. Damit schaffen wir Momente der Freude für alle Beteiligten und geben uns gleichzeitig den Ansporn, das DBM in unser alle Sinne weiterzuentwickeln. Gelegenheiten und Möglichkeiten gibt es viele. Inspirationen finden Sie auf Seite 25.
Die nun vorliegende Weihnachtsausgabe der DBM Facts steht ganz im Zeichen von Afrika. Irene Hösli setzt mit ihrem Artikel über ihren Einsatz in Tansania, wo sie zwei Wochen ganz im Sinne des Weihnachtsgedankens Geburtshilfe geleistet hat, die Reihe fort, die Thomas Klimkait in der letzten Ausgabe begonnen hat. Auf die andere Seite des Kontinents reisen wir mit Frederick Bright, der uns einlädt, mit ihm das Christfest in Ghana zu feiern.
Die aktuellsten Publikationen finden ab Seite 10, gefolgt von vielem anderen mehr.

Frohe Festtage!
Radek Skoda

Dear Readers,

For most of us, the turn of the year is a chance to review the year just gone by. As this year draws to a close I have heard the phrase "Happy DBM" from many sides, and I hope that it will remain so for a long time. However, we also need to look ahead: there are many scientific, strategic and organizational challenges to overcome in the years to come. Success essentially depends on the people who work at the DBM and who make up the DBM. We should be conscious of those around us and the work they do. In this way, we create moments of joy for all concerned and at the same time provide the incentive to further develop the DBM in all our minds. There are many opportunities. Inspiration can be found on page 25.
The present Christmas edition of DBM Facts is all about Africa. Irene Hösli's article about her assignment in Tanzania, where she spent two weeks in the spirit of the Christmas concept of obstetrics, continues the series that Thomas Klimkait started in the last issue.
We travel to the other side of the continent with Frederick Bright, who has invited us to celebrate a Christmas in Ghana with him. The most recent publications can be found from page 10 onward, followed by lots, lots more.

Happy Holidays!
Radek Skoda

Vertrauen, Lachen und viel Arbeit

Geburtshilflicher Alltag in Tansania

Eingang Kitete Referral Hospital

Die Klinische Arbeit in einem Perinatalzentrum in der Schweiz und in einem Referral Hospital in Tansania könnte nicht unterschiedlicher sein und hat doch viele Ähnlichkeiten. Der Beitrag soll einen Einblick in den geburtshilflichen Alltag in einem ostafrikanischen Spital geben.

Das Kitete Referral Hospital in Tabora liegt mehr als 1000 km entfernt von Daressalam im tansanischen Binnenland auf 1200 m Höhe. Es gibt weder interessante Safaritouren noch besondere Sehenswürdigkeiten in dieser Stadt, die im 18. Jahrhundert an der Karawanenstrasse vom Kongo zum indischen Ozean lag und für den ostafrikanischen Sklavenhandel bekannt war.
Die ca. 300 000 Einwohner leben meistens von Kleinstbetrieben. Tabak und Erdnüsse werden angebaut und exportiert. Im ausgehenden 19. Jahrhundert spielte es bis zum ersten Weltkrieg für kurze Zeit eine wichtige Rolle als Verkehrsknotenpunkt, als die deutschen Kolonialherren Tabora zur Hauptstadt in der Kolonie «Südostafrika» machten und ein bereits bestehendes Eisenbahnnetz ausbauten. Hier kreuzten sich die Züge von Nord nach Süd zwischen dem Victoriasee und Sambia und von Ost

Karte von Tansania

Bahnhof Tabora

Areal Kitete Hospital

nach West zwischen Daressalam und dem Tanganika See. Der historische Bahnhof steht noch heute und ist für uns bei jedem Einsatz eine Attraktion. Neben Händlern und Köchen, die improvisierte Essensstände aufstellen, warten viele Menschen voll bepackt auf einen Zug, der sich mehr oder weniger an den Fahrplan hält. Für den Kaiser wurde sogar ein Bahnhofshotel in Form eines kleinen Jagdschlösschens erbaut. Es kam nicht mehr zum kaiserlichen Besuch, da Deutschland seine Kolonie im ersten Weltkrieg abtreten musste. Das Schlösschen steht aber noch und ist das einzig akzeptable Hotel im Ort.

Auf dem Weg zum Morgenrapport fällt der Blick auf den schönen Frangipani Baum, dessen heruntergefallene Blüten und Blätter jeden Tag von einer Angestellten des Spitals weggefegt werden. Der Rapport findet eigentlich um 7.45 Uhr in einem Einzimmerhaus mit offenen Fenstern und Türen statt, nur halten sich die wenigsten dran. Es wird von den Notfallaufnahmen der Nacht aus allen Abteilungen berichtet. Die meisten Ärzte, Medical Officer, administrativ tätige Personen und «Nurses» sind heute nicht anwesend. Die aktuelle Bettenbelegung, die Anzahl verstorbener Patienten und der Vorrat an Bluttransfusionen wird vorgelesen.

Der Gebärsaal ist an diesem Morgen komplett gefüllt. Zwei Notfälle liegen auf dem Boden. Von einem externen Health Center wurde eine Frau mit schwerer postpartaler Blutung gerade noch rechtzeitig verlegt, sie erhält Bluttransfusionen, was dank Labor und Blutbank in diesem Spital möglich ist. Allerdings müssen die Angehörigen für Katheter, Medikamente und die Transfusion aufkommen, gratis ist nur die Geburt. Eine andere Schwangere hatte einen Krampfanfall, eine Eklampsie, zuhause. Nun wird sie standartgerecht mit Magnesium therapiert.

Gebärsaal

Einlingsgeburt

Zwillingsfrühgeburten

Drillingsgeburt

Der Ultraschall zeigt, dass das Kind noch lebt, aber eine Wachstumsrestriktion hat. Dank einer schweizerischen Stiftung konnten bisher mehrere Hebammen und Ärzte eine Basisausbildung in geburtshilflichem Ultraschall im Norden von Tansania machen, geleitet von der Schweizerischen Stiftung für medizinischen Wissenstransfer. Sie können pränatal wenigstens die Anzahl Feten, die Lage und Vitalität, das Gestationsalter und die Lage der Placenta beurteilen.

Zwillingsschwangerschaften sind in Tansania wesentlich häufiger als bei uns und im Gegensatz zu hier häufig vor der Geburt nicht bekannt. Drillingsschwangerschaften sind aber auch in Tansania selten und so ist verständlich, dass auch unsere Hebammen strahlen, als diese Drillinge überraschend aber gesund und wohlbehalten auf die Welt gekommen sind. Das ist nicht selbstverständlich, da ca. 19 von 1000 Lebendgeburten peripartal versterben oft an Asphyxie, Frühgeburt, Sepsis oder Fehlbildungen. Im Vergleich: Die neonatale Mortalität liegt in der Schweiz bei 3 – 4 pro 1000 Geburten.

Abgetrennt durch Metallwände liegen in Kojen Gebärende, die selber ihre «Kangas», grosse bunte Tücher, zur Geburt mitgebracht haben. Nach der Geburt werden sie das Neugeborene in Tücher einwickeln, alles selber zusammenpacken müssen und dann für ca. 24 Stunden noch aufs

Familienangehörige, die Essen bringen

Im Operationssaal

Wochenbett gehen. Die Angehörigen warten draussen und bringen das Essen. Die Geburtsbetten sind ebenfalls mit Hilfe des USB gekauft worden, die Betten auf dem Wochenbett und der Pränatalstation standen früher im USB. Die Erstversorgung der Neugeborenen wird grösstenteils von den Hebammen durchgeführt.

Die Sectiorate von ca. 18% ist gestiegen und für tansanische Verhältnisse hoch, bezogen auf das Risikokollektiv im Kitete jedoch gering. Zwischen 4000 und 6000 Geburten finden hier jährlich statt, abhängig davon, wie die Versorgung in der Peripherie ist. Bisher gibt es keinen Facharzt für Gynäkologie und Geburtshilfe, zwei Ärzte werden zurzeit in Daressalam ausgebildet – mit einer schweizerischen Stiftung. Die Geburten werden von Hebammen und Nurses durchgeführt, auch komplizierte Beckenendlagen, Nachtastungen und natürlich die Reanimation von Neugeborenen. Bei Verdacht auf fetal distress, schlechte Herztöne unter der Geburt steht eine zügige Geburt an, die im angrenzenden Operationstrakt durchgeführt wird. Die Kaiserschnitte oder gynäkologische Operationen werden von Ärzten oder Assistant Medical Officers, angelernten Ärzten, durchgeführt. Einer von uns Ärzten wird assistieren, zuvor aber vor allem darauf drängen, dass alles schnell organisiert wird. Der neue Operationstrakt hat ein dichtes Dach, im alten regnete es sogar auf die sterilisierten Instrumente und Op-Tücher. Die Arbeit im Operationssaal ist herausfordernd, es gibt nur catgut, Nahtmaterial, das wesentlich dicker ist, die Nadelhalter und Pinzetten greifen nicht exakt, die Nadel rutscht leicht ab. Aber immerhin funktioniert der Strom, gelegentlich gibt es auch Stromausfälle und der Spitalgenerator springt nicht immer an. Die Operationstücher werden selber genäht und an der Luft getrocknet.

Neben der antepartalen Station gibt es eine Wochenbettstation nach vaginaler Geburt und eine nach Sectio sowie ein Bonding Zimmer für Frauen, die mit ihren zu frühgeborenen Kindern oft Wochen im Spital bleiben. Die Intensivstation ist weit weg vom Gebärsaal und ist sehr häufig personell unterbesetzt. Am Nachmittag gibt es auch ambulante Sprechstunden, zu denen Frauen mit unerfülltem Kinderwunsch, Blutungsstörungen oder mit Abszessen in der Sectionaht kommen.

Operationstücher werden getrocknet

Simulationsszenarien

Teaching

Arbeiten an den ewig defekten Waschmaschinen

Stromversorgung

Schreinerarbeiten

In unserem zwei- bis dreiwöchigen klinischen Einsatz, der zweimal pro Jahr stattfindet, arbeitet unser Team, bestehend aus Hebammen, Ärzten und einem Medizintechniker Hand in Hand mit den tansanischen Kollegen. Sie unterstützen bei Geburten, helfen aber auch beim Putzen und Auffüllen. Im Rahmen des teachings geben wir Vorträge zu aktuellen Themen, die wir gemeinsam planen. Wir trainieren in Simulationsübungen die typischen Notfallsituationen wie Präeklampsie, postpartale Blutung, vaginal operative Geburten oder Neugeborenen-Reanimation. Anhand der Aufarbeitung interner Fälle regen wir ein Debriefing an, bei dem es um die Verbesserung der Diagnosestellung, der korrekten Ausführung von Massnahmen und der adäquaten Dokumentation geht. «Too little, too late», das ist sowohl bei uns als auch in Tabora häufig der Grund für Substandard care. Den Techniker sehen wir tagsüber mit seiner Mannschaft über das ganze Spitalareal laufen und Reparaturarbeiten durchführen, ab und zu hilft er auch bei uns mit.

Besuch auf dem Markt

Ziel der Arbeit ist eine Verbesserung der maternalen und neonatalen Versorgung, aber auch ein Austausch verschiedener Kulturen, ein Einblick, wie Geburtshilfe an vielen Orten auf der Welt stattfindet. Die regelmässigen Einsätze führen zu gegenseitigem Vertrauen, wir lachen viel miteinander, aber arbeiten auch intensiv und verantwortungsbewusst. Die maternale Mortalität im Kitete Hospital ist im Lauf des letzten Jahres gesunken, das berichten die Mitarbeiter sehr stolz. Wohl nur teilweise ein Resultat unserer Bemühungen und wenn dann wegen einem veränderten Problembewusstsein der lokalen Mitarbeitenden. Die Notfallversorgung klappt inzwischen sehr gut, eigentlich so wie bei uns.

Irene Hösli und André Kind

Das gesamte Team

Hebammen: Samira Akra, Andrea Ankli, Danielle Barth, Sonja Bruttel, Cecilia Gebhart, Martina Gisin, Iris Hochstrasser, Giovaninva Meola, Miriam Zoller

Technik: Volker Brunner, Roland Enzler, Patrick Rinderknecht, Manfred Stephan

Ärztinnen/Ärzte: Astrid Ahler, Reta Bossi, Maya Brunner, Johanna Büchel, Brigitte Frey-Tirri, Viola Heinzelmann, Linda Herberich, Irene Hösli, André Kind, Leonie Matt, Cécile Monod, Heidrun Schönberger, Eva Sift, Albert Urwyler, Heike Willi

Dissertationen

Am 7. Mai 2019 konnte **Deborah Rudin** von der Forschungsgruppe "Clinical Pharmacology" (Departement Biomedizin Hebelstrasse) ihre Dissertation mit Erfolg beenden. Sie befasste sich in ihrer Doktorarbeit mit dem Thema: "Toxicological and Clinical Investigations of Metamizole-Associated Neutropenia".

Auszeichnungen

Venia docendi verliehen

In ihrer Sitzung am 15. Mai 2019 hat die Regenz der Universität Basel **Marcus Mumme** von der Forschungsgruppe „Tissue Engineering" (Departement Biomedizin Hebelstrasse) die Venia docendi für «Orthopädie und Traumatologie» verliehen. **Anne-Katrin Pröbstel** von der Forschungsgruppe «Clinical Neuroimmunology» erhielt die Lehrbefugnis für Neurologie. Sie sind damit befugt, den Titel Privatdozent/in zu führen.

Titularprofessuren für Gabriela Kuster Pfister, Arnaud Scherberich und Adrian Egli

Der Unirat der Universität Basel hat in seiner Sitzung vom 31. Oktober 2019 die Ernennungen von **Gabriela Kuster Pfister** von der Forschungsgruppe «Myocardial Research» (Departement Biomedizin Hebelstrasse) zur Titularprofessorin für Kardiologie, **Arnaud Scherberich** von der Forschungsgruppe «Tissue Engineering» (Departement Biomedizin Hebelstrasse) und **Adrian Egli** von der Forschungsgruppe «Applied Microbiology Research» (Departement Biomedizin Hebelstrasse) zu Titularprofessoren für Experimentelle Medizin durch die Regenz genehmigt.

Dino Lüthi und Salvatore Piscuoglio ausgezeichnet

Dino Lüthi von der Forschungsgruppe «Psychopharmacology Research» (Departement Biomedizin Hebelstrasse) hat den Young Scientist Award 2019 der Swiss Society of Clinical Pharmacology and Toxicology erhalten.

Salvatore Piscuoglio von der Forschungsgruppe «Visceral Surgery» (Departement Biomedizin Hebelstrasse) hat von der Swiss Foundation against Liver Cancer den diesjährigen Preis für seine Publikation «Genetic profiling using plasma-derived cell-free DNA in therapy-naïve hepatocellular carcinoma patients: a pilot study» erhalten. Der Preis wurde ihm am 5. Dezember 2019 beim jährlichen HCC day in Lausanne überreicht.

Herzliche Gratulation!

Department of Biomedicine Research Day 2020

Thursday, January 16, 08:00 – 13:15 h
Small Lecture Hall, Zentrum für Lehre und Forschung
Hebelstrasse 20, 4031 Basel

Speakers

Josef Bischofberger
Gennaro De Libero
Magdalena Filipowicz Sinnreich
Viola Heinzelmann
Gregor Hutter
Ivan Martin
Tania Rinaldi Barkat
Jürg Schwaller
Volker Spindler

Departement Biomedizin Basel

image courtesy of Anne-Catherine Feutz, De Geyter Lab

Nature Vol. 572, 254–259(2019) IF 43.070

Absence of NKG2D ligands defines leukaemia stem cells and mediates their immune evasion

Anna M. Paczulla[1,21], Kathrin Rothfelder[2,3,4,21], Simon Raffel[5,6,7,21], Martina Konantz[1], Julia Steinbacher[2,3], Hui Wang[1], Claudia Tandler[2,3,4], Marcelle Mbarga[1], Thorsten Schaefer[1], Mattia Falcone[5,6], Eva Nievergall[5,6], Daniela Dörfel[3], Pauline Hanns[1], Jakob R. Passweg[8], Christoph Lutz[7], Juerg Schwaller[1,9], Robert Zeiser[10,11], Bruce R. Blazar[12], Michael A. Caligiuri[13,14,15], Stephan Dirnhofer[16], Pontus Lundberg[17], Lothar Kanz[3], Leticia Quintanilla-Martinez[18], Alexander Steinle[19], Andreas Trumpp[5,6,20,22], Helmut R. Salih[2,3,4,22*] & Claudia Lengerke[1,8,22]

Patients with acute myeloid leukaemia (AML) often achieve remission after therapy, but subsequently die of relapse[1] that is driven by chemotherapy-resistant leukaemic stem cells (LSCs)[2,3]. LSCs are defined by their capacity to initiate leukaemia in immunocompromised mice[4]. However, this precludes analyses of their interaction with lymphocytes as components of anti-tumour immunity[5], which LSCs must escape to induce cancer. Here we demonstrate that stemness and immune evasion are closely intertwined in AML. Using xenografts of human AML as well as syngeneic mouse models of leukaemia, we show that ligands of the danger detector NKG2D — a critical mediator of anti-tumour immunity by cytotoxic lymphocytes, such as NK cells[6,7,8,9] — are generally expressed on bulk AML cells but not on LSCs. AML cells with LSC properties can be isolated by their lack of expression of NKG2D ligands (NKG2DLs) in both CD34-expressing and non-CD34-expressing cases of AML. AML cells that express NKG2DLs are cleared by NK cells, whereas NKG2DL-negative leukaemic cells isolated from the same individual escape cell killing by NK cells. These NKG2DL-negative AML cells show an immature morphology, display molecular and functional stemness characteristics, and can initiate serially re-transplantable leukaemia and survive chemotherapy in patient-derived xenotransplant models. Mechanistically, poly-ADP-ribose polymerase 1 (PARP1) represses expression of NKG2DLs. Genetic or pharmacologic inhibition of PARP1 induces NKG2DLs on the LSC surface but not on healthy or pre-leukaemic cells. Treatment with PARP1 inhibitors, followed by transfer of polyclonal NK cells, suppresses leukaemogenesis in patient-derived xenotransplant models. In summary, our data link the LSC concept to immune escape and provide a strong rationale for targeting therapy-resistant LSCs by PARP1 inhibition, which renders them amenable to control by NK cells in vivo.

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Advanced Materials 2019, 1808050 IF 25.809

Mechanically Defined Microenvironment Promotes Stabilization of Microvasculature, Which Correlates with the Enrichment of a Novel Piezo-1$^+$ Population of Circulating CD11b$^+$/CD115$^+$ Monocytes

Aurelien Forget, Roberto Gianni-Barrera, Andrea Uccelli, Melika Sarem, Esther Kohler, Barbara Fogli, Manuele G. Muraro, Sandrine Bichet, Konrad Aumann, Andrea Banfi, and V. Prasad Shastri

Abstract

Vascularization is a critical step in the restoration of cellular homeostasis. Several strategies including localized growth factor delivery, endothelial progenitor cells, genetically engineered cells, gene therapy, and prevascularized implants have been explored to promote revascularization. But, long-term stabilization of newly induced vessels remains a challenge. It has been shown that fibroblasts and mesenchymal stem cells can stabilize newly induced vessels. However, whether an injected biomaterial alone can serve as an instructive environment for angiogenesis remains to be elucidated. It is reported here that appropriate vascular branching, and long-term stabilization can be promoted simply by implanting a hydrogel with stiffness matching that of fibrin clot. A unique subpopulation of circulating CD11b$^+$ myeloid and CD11b$^+$/CD115$^+$ monocytes that express the stretch activated cation channel Piezo-1, which is enriched prominently in the clot-like hydrogel, is identified. These findings offer evidence for a mechanobiology paradigm in angiogenesis involving an interplay between mechanosensitive circulating cells and mechanics of tissue microenvironment.

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SDHA gain-of-function engages inflammatory mitochondrial retrograde signaling via KEAP1–Nrf2

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Abstract

Whether screening the metabolic activity of immune cells facilitates discovery of molecular pathology remains unknown. Here we prospectively screened the extracellular acidification rate as a measure of glycolysis and the oxygen consumption rate as a measure of mitochondrial respiration in B cells from patients with primary antibody deficiency. The highest oxygen consumption rate values were detected in three study participants with persistent polyclonal B cell lymphocytosis (PPBL). Exome sequencing identified germline mutations in *SDHA*, which encodes succinate dehydrogenase subunit A, in all three patients with PPBL. SDHA gain-of-function led to an accumulation of fumarate in PPBL B cells, which engaged the KEAP1–Nrf2 system to drive the transcription of genes encoding inflammatory cytokines. In a single patient trial, blocking the activity of the cytokine interleukin-6 in vivo prevented systemic inflammation and ameliorated clinical disease. Overall, our study has identified pathological mitochondrial retrograde signaling as a disease modifier in primary antibody deficiency.

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Hyperphysiological compression of articular cartilage induces an osteoarthritic phenotype in a cartilage-on-a-chip model

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Abstract

Owing to population aging, the social impact of osteoarthritis (OA)—the most common musculoskeletal disease—is expected to increase dramatically. Yet, therapy is still limited to palliative treatments or surgical intervention, and disease-modifying OA (DMOA) drugs are scarce, mainly because of the absence of relevant preclinical OA models. Therefore, in vitro models that can reliably predict the efficacy of DMOA drugs are needed. Here, we show, using a newly developed microphysiological cartilage-on-a-chip model that enables the application of strain-controlled compression to three-dimensional articular cartilage microtissue, that a 30% confined compression recapitulates the mechanical factors involved in OA pathogenesis and is sufficient to induce OA traits. Such hyperphysiological compression triggers a shift in cartilage homeostasis towards catabolism and inflammation, hypertrophy, and the acquisition of a gene expression profile akin to those seen in clinical osteoarthritic tissue. The cartilage on-a-chip model may enable the screening of DMOA candidates.

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GEF-H1 Signaling upon Microtubule Destabilization Is Required for Dendritic Cell Activation and Specific Anti-tumor Responses

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SUMMARY

Dendritic cell (DC) activation is a critical step for anti-tumor T cell responses. Certain chemotherapeutics can influence DC function. Here we demonstrate that chemotherapy capable of microtubule destabilization has direct effects on DC function; namely, it induces potent DC maturation and elicits anti-tumor immunity. Guanine nucleotide exchange factor-H1 (GEF-H1) is specifically released upon microtubule destabilization and is required for DC activation. In response to chemotherapy, GEF-H1 drives a distinct cell signaling program in DCs dominated by the c-Jun N-terminal kinase (JNK) pathway and AP-1/ATF transcriptional response for control of innate and adaptive immune responses. Microtubule destabilization, and subsequent GEF-H1 signaling, enhances cross-presentation of tumor antigens to CD8 T cells. In absence of GEF-H1, anti-tumor immunity is hampered. In cancer patients, high expression of the GEF-H1 immune gene signature is associated with prolonged survival. Our study identifies an alternate intracellular axis in DCs induced upon microtubule destabilization in which GEF-H1 promotes protective anti-tumor immunity.

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Naegeli-Franceschetti-Jadassohn syndrome and dermatopathia pigmentosa reticularis: intrafamilial overlap of phenotypes in patients with the same *KRT*$_{14}$ frameshift variant

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DEAR EDITOR, Naegeli–Franceschetti–Jadassohn syndrome (NFJS; OMIM 161000) and dermatopathia pigmentosa reticularis (DPR; OMIM 125595) have been defined as separate ectodermal dysplasias. Only 55 patients from nine families with NFJS and 21 patients with DPR have been published in the literature. Common to both diseases are anhidrosis/hypohidrosis and a reticular pattern of hyperpigmentation of the skin (Table 1).[1] Furthermore, most patients have palmoplantar keratoderma (PPK), hypoplasia to aplasia of dermatoglyphics and onychodystrophy. Individual patients show nonscarring blisters on the hands and feet during the first years of life. Debated differences between NFJS and DPR are fading of reticular hyperpigmentation and defects of teeth and enamel in patients with NFJS, whereas partial noncicatricial alopecia of the scalp and eyebrows have been assigned to DPR.[2] Both NFJS and DPR are caused by heterozygous nonsense or frameshift variants of the first few codons in the gene for keratin 14 (KRT14) and were therefore considered as allelic diseases.[3] Four different causative genetic variants in five NFJS families and one DPR family have been reported, all resulting in a truncated reading frame within the sequence encoding the head domain of the KRT14 protein (Table 1). We examined a previously unreported five-generation family with NFJS originating from Switzerland, with nine affected individuals. The study was approved by local ethics committees (EKNZ 2015-390 and KEK BE 322/15).

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Quantitative proteomics reveals reduction of endocytic machinery components in gliomas

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Background Gliomas are the most frequent and aggressive malignancies of the central nervous system. Decades of molecular analyses have demonstrated that gliomas accumulate genetic alterations that culminate in enhanced activity of receptor tyrosine kinases and downstream mediators. While the genetic alterations, like gene amplification or loss, have been well characterized, little information exists about changes in the proteome of gliomas of different grades.

Methods We performed unbiased quantitative proteomics of human glioma biopsies by mass spectrometry followed by bioinformatic analysis.

Findings Various pathways were found to be up- or downregulated. In particular, endocytosis as pathway was affected by a vast and concomitant reduction of multiple machinery components involved in initiation, formation, and scission of endocytic carriers. Both clathrin-dependent and -independent endocytosis were changed, since not only clathrin, AP-2 adaptins, and endophilins were downregulated, but also dynamin that is shared by both pathways. The reduction of endocytic machinery components caused increased receptor cell surface levels, a prominent phenotype of defective endocytosis. Analysis of additional biopsies revealed that depletion of endocytic machinery components was a common trait of various glioma grades and subclasses.

Interpretation We propose that impaired endocytosis creates a selective advantage in glioma tumor progression due to prolonged receptor tyrosine kinase signaling from the cell surface.

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Tumor-derived TGF-β inhibits mitochondrial respiration to suppress IFN-γ production by human CD4⁺ T cells

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Abstract

Transforming growth factor–β (TGF-β) is produced by tumors, and increased amounts of this cytokine in the tumor microenvironment and serum are associated with poor patient survival. TGF-β–mediated suppression of antitumor T cell responses contributes to tumor growth and survival. However, TGF-β also has tumor-suppressive activity; thus, dissecting cell type–specific molecular effects may inform therapeutic strategies targeting this cytokine. Here, using human peripheral and tumor-associated lymphocytes, we investigated how tumor-derived TGF-β suppresses a key antitumor function of CD4⁺ T cells, interferon-γ (IFN-γ) production. Suppression required the expression and phosphorylation of Smad proteins in the TGF-β signaling pathway, but not their nuclear translocation, and depended on oxygen availability, suggesting a metabolic basis for these effects. Smad proteins were detected in the mitochondria of CD4⁺ T cells, where they were phosphorylated upon treatment with TGF-β. Phosphorylated Smad proteins were also detected in the mitochondria of isolated tumor-associated lymphocytes. TGF-β substantially impaired the ATP-coupled respiration of CD4⁺ T cells and specifically inhibited mitochondrial complex V (ATP synthase) activity. Last, inhibition of ATP synthase alone was sufficient to impair IFN-γ production by CD4⁺ T cells. These results, which have implications for human antitumor immunity, suggest that TGF-β targets T cell metabolism directly, thus diminishing T cell function through metabolic paralysis.

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Emerging anaerobic and partially acid-fast *Lawsonella clevelandensis*: extended characterization by antimicrobial susceptibility testing and whole genome sequencing¤

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Lawsonella clevelandensis is an emerging pathogenic bacterium taxonomically described in 2016 [1]. The organism is very slow growing, Gram variable, partially acid fast and facultatively anaerobic. Between 2013 and 2018 a total of eight cases, six from North America and two from Europe, have been reported [2–4]. All cases showed abscess formation with a single bacterial infection in different body sites. To date no antimicrobial susceptibility testing (AST) has been performed on this highly fastidious microorganism, and its normal habitat is unclear. In this report, minimum inhibitory concentrations (MICs) of diverse antimicrobial agents against L. clevelandensis were determined for the !rst time. In addition, whole genome sequencing (WGS) was performed from our isolate, and retrospective sequence analyses indicate that this novel organism could represent a member of the normal human microbiota.

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Enhanced Dendritic Inhibition and Impaired NMDAR Activation in a Mouse Model of Down Syndrome

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Abstract

Down syndrome (DS) or Trisomy 21 is a developmental disorder leading to cognitive deficits, including disruption of hippocampus-dependent learning and memory. Enhanced inhibition has been suggested to underlie these deficits in DS based on studies using the Ts65Dn mouse model. Here we show that, in this mouse model, GABAergic synaptic inhibition onto dendrites of hippocampal pyramidal cells is increased. By contrast, somatic inhibition was not altered. In addition, synaptic NMDAR currents were reduced. Furthermore, dendritic inhibition was mediated via nonlinear α5-subunit containing $GABA_A$Rs that closely matched the kinetics and voltage dependence of NMDARs. Thus, enhanced dendritic inhibition and reduced NMDA currents strongly decreased burst-induced NMDAR-mediated depolarization and impaired LTP induction. Finally, selective reduction of α5-$GABA_A$R-mediated inhibition rescued both burst-induced synaptic NMDAR activation and synaptic plasticity. These results demonstrate that reduced synaptic NMDAR activation and synaptic plasticity in the Ts65Dn mouse model of DS can be corrected by specifically targeting nonlinear dendritic inhibition.

Significance Statement

Mild to moderate intellectual disability is a prominent feature of Down syndrome. Previous studies in mouse models suggest that increased synaptic inhibition is a main factor for decreased synaptic plasticity, the cellular phenomenon underlying memory. The present study shows that increased inhibition specifically onto dendrites together with reduced NMDAR content in excitatory synapses may be the cause. Reducing a slow nonlinear component that is specific to dendritic inhibitory inputs and mediated by α5 subunit-containing $GABA_A$ receptors rescues both NMDAR activation and synaptic plasticity.

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A Conformational Restriction Strategy for the Identification of a Highly Selective Pyrimido-pyrrolo-oxazine mTOR Inhibitor

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Abstract

The mechanistic target of rapamycin (mTOR) plays a pivotal role in growth and tumor progression and is an attractive target for cancer treatment. ATP-competitive mTOR kinase inhibitors (TORKi) have the potential to overcome limitations of rapamycin derivatives in a wide range of malignancies. Herein, we exploit a conformational restriction approach to explore a novel chemical space for the generation of TORKi. Structure–activity relationship (SAR) studies led to the identification of compound 12b with a ~450-fold selectivity for mTOR over class I PI3K isoforms. Pharmacokinetic studies in male Sprague Dawley rats highlighted a good exposure after oral dosing and a minimum brain penetration. CYP450 reactive phenotyping pointed out the high metabolic stability of 12b. These results identify the tricyclic pyrimido-pyrrolo-oxazine moiety as a novel scaffold for the development of highly selective mTOR inhibitors for cancer treatment.

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Molecular signatures identify immature mesenchymal progenitors in early mouse limb buds that respond differentially to morphogen signaling

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Abstract

The key molecular interactions governing vertebrate limb bud development are a paradigm for studying the mechanisms controlling progenitor cell proliferation and specification during vertebrate organogenesis. However, little is known about the cellular heterogeneity of the mesenchymal progenitors in early limb buds that ultimately contribute to the chondrogenic condensations prefiguring the skeleton. We combined flow cytometric and transcriptome analyses to identify the molecular signatures of several distinct mesenchymal progenitor cell populations present in early mouse forelimb buds. In particular, jagged 1 (JAG1)-positive cells located in the posterior-distal mesenchyme were identified as the most immature limb bud mesenchymal progenitors (LMPs), which crucially depend on SHH and FGF signaling in culture. The analysis of gremlin 1 (*Grem1*)- deficient forelimb buds showed that JAG1-expressing LMPs are protected from apoptosis by GREM1-mediated BMP antagonism. At the same stage, the osteo-chondrogenic progenitors (OCPs) located in the core mesenchyme are already actively responding to BMP signaling. This analysis sheds light on the cellular heterogeneity of the early mouse limb bud mesenchyme and on the distinct response of LMPs and OCPs to morphogen signaling.

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NLRP6 Deficiency in CD4 T Cells Decreases T Cell Survival Associated with Increased Cell Death

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Abstract

The nucleotide-binding oligomerization domain (NOD)-like receptors belong to the family of pattern recognition receptors (PRRs). NOD-like receptors play a role in regulation of innate immune response by recognition of both pathogen-associated molecular patterns that are engulfed during phagocytic process and danger-associated molecular patterns that are mainly byproducts of cell stress mediated response. NOD-like family pyrin domain containing 6 (NLRP6) is one of the 14 pyrin domain–containing receptors. NLRP6 is highly expressed by epithelial and goblet cells to regulate epithelial renewal and mucus production in mice and humans, but its function in T cells is rather unknown. Increased caspase-1 activation and cell death were observed in mouse *Nlrp6*–deficient T cells following adoptive transfer into *Rag2*-deficient mice, indicating that *Nlrp6* deficiency in $CD4^+$ T cells led to decreased survival.

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Quantitative RyR1 reduction and loss of calcium sensitivity of RyR1Q1970fsX16+A4329D cause cores and loss of muscle strength

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Abstract

Recessive ryanodine receptor 1 (RYR1) mutations cause congenital myopathies including multiminicore disease (MmD), congenital fiber-type disproportion and centronuclear myopathy. We created a mouse model knocked-in for the Q1970fsX16+A4329D RYR1 mutations, which are isogenic with those identified in a severely affected child with MmD. During the first 20 weeks after birth the body weight and the spontaneous running distance of the mutant mice were 20% and 50% lower compared to wild-type littermates. Skeletal muscles from mutant mice contained 'cores' characterized by severe myofibrillar disorganization associated with misplacement of mitochondria. Furthermore, their muscles developed less force and had smaller electrically evoked calcium transients. Mutant RyR1 channels incorporated into lipid bilayers were less sensitive to calcium and caffeine, but no change in single-channel conductance was observed. Our results demonstrate that the phenotype of the RyR1Q1970fsX16+A4329D compound heterozygous mice recapitulates the clinical picture of multiminicore patients and provide evidence of the molecular mechanisms responsible for skeletal muscle defects.

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Aberrant regulation of epigenetic modifiers contributes to the pathogenesis in patients with selenoprotein N-related myopathies

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Congenital myopathies are early onset, slowly progressive neuromuscular disorders of variable severity. They are genetically and phenotypically heterogeneous and caused by pathogenic variants in several genes. Multiminicore Disease, one of the more common congenital myopathies, is frequently caused by recessive variants in either SELENON, encoding the endoplasmic reticulum glycoprotein selenoprotein N or RYR1, encoding a protein involved in calcium homeostasis and excitation–contraction coupling. The mechanism by which recessive SELENON variants cause Multiminicore disease (MmD) is unclear. Here, we extensively investigated muscle physiological, biochemical and epigenetic modifications, including DNA methylation, histone modification, and noncoding RNA expression, to understand the pathomechanism of MmD. We identified biochemical changes that are common in patients harboring recessive RYR1 and SELENON variants, including depletion of transcripts encoding proteins involved in skeletal muscle calcium homeostasis, increased levels of Class II histone deacetylases (HDACs) and DNA methyltransferases. CpG methylation analysis of genomic DNA of patients with RYR1 and SELENON variants identified >3,500 common aberrantly methylated genes, many of which are involved in calcium signaling. These results provide the proof of concept for the potential use of drugs targeting HDACs and DNA methyltransferases to treat patients with specific forms of congenital myopathies.

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Extraocular muscle function is impaired in *ryr3*$^{-/-}$ mice

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Abstract

Calcium is an ubiquitous second messenger mediating numerous physiological processes, including muscle contraction and neuronal excitability. Ca^{2+} is stored in the ER/SR and is released into the cytoplasm via the opening of intracellular inositol trisphosphate receptor and ryanodine receptor calcium channels. Whereas in skeletal muscle, isoform 1 of the RYR is the main channel mediating calcium release from the SR leading to muscle contraction, the function of ubiquitously expressed ryanodine receptor 3 (RYR3) is far from clear; it is not known whether RYR3 plays a role in excitation–contraction coupling. We recently reported that human extraocular muscles express high levels of RYR3, suggesting that such muscles may be useful to study the function of this isoform of the Ca^{2+} channel. In the present investigation, we characterize the visual function of *ryr3*$^{-/-}$ mice. We observe that ablation of RYR3 affects both mechanical properties and calcium homeostasis in extraocular muscles. These changes significantly impact vision. Our results reveal for the first time an important role for RYR3 in extraocular muscle function.

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Metabolites of the ring-substituted stimulants MDMA, methylone and MDPV differentially affect human monoaminergic systems

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Background: Amphetamine analogs with a 3,4-methylenedioxy ring-substitution are among the most popular illicit drugs of abuse, exerting stimulant and entactogenic effects. Enzymatic *N*-demethylation or opening of the 3,4-methylenedioxy ring via *O*-demethylenation gives rise to metabolites that may be pharmacologically active. Indeed, previous studies in rats show that specific metabolites of 3,4-methylenedioxymethamphetamine (MDMA), 3,4-methylenedioxymethcathinone (methylone) and 3,4-methylenedioxypyrovalerone (MDPV) can interact with monoaminergic systems. **Aim:** Interactions of metabolites of MDMA, methylone and MDPV with human monoaminergic systems were assessed. **Methods:** The ability of parent drugs and their metabolites to inhibit uptake of tritiated norepinephrine, dopamine and serotonin (5-HT) was assessed in human embryonic kidney 293 cells transfected with human monoamine transporters. Binding affinities and functional activity at monoamine transporters and various receptor subtypes were also determined. **Results:** MDMA and methylone displayed greater potency to inhibit norepinephrine uptake as compared to their effects on dopamine and 5-HT uptake. *N*-demethylation of MDMA failed to alter uptake inhibition profiles, whereas *N*-demethylation of methylone decreased overall transporter inhibition potencies. *O*-demethylenation of MDMA, methylone and MDPV resulted in catechol metabolites that maintained norepinephrine and dopamine uptake inhibition potencies, but markedly reduced activity at 5-HT uptake. *O*-methylation of the catechol metabolites significantly decreased norepinephrine uptake inhibition, resulting in metabolites lacking significant stimulant properties. **Conclusions:** Several metabolites of MDMA, methylone and MDPV interact with human transporters and receptors at pharmacologically relevant concentrations. In particular, *N*-demethylated metabolites of MDMA and methylone circulate in unconjugated form and could contribute to the in vivo activity of the parent compounds in human users.

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Exogenous Iron Increases Fasciocidal Activity and Hepatocellular Toxicity of the Synthetic Endoperoxides OZ78 and MT04

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Abstract

The synthetic peroxides OZ78 and MT04 recently emerged as fasciocidal drug candidates. However, the effect of iron on fasciocidal activity and hepatocellular toxicity of these compounds is unknown. We investigated the in vitro fasciocidal activity and hepatocellular toxicity of OZ78 and MT04 in absence and presence of Fe(II)chloride and hemin, and conducted a toxicological study in mice. Studies were performed in comparison with the antimalarial artesunate (AS), a semisynthetic peroxide. Fasciocidal effects of OZ78 and MT04 were confirmed and enhanced by Fe^{2+} or hemin. In HepG2 cells, AS reduced cellular ATP and impaired membrane integrity concentration-dependently. In comparison, OZ78 or MT04 were not toxic at 100 µM and reduced the cellular ATP by 13% and 19%, respectively, but were not membrane-toxic at 500 µM. The addition of Fe^{2+} or hemin increased the toxicity of OZ78 and MT04 significantly. AS inhibited complex I, II, and IV of the mitochondrial electron transport chain, and MT04 impaired complex I and II, whereas OZ78 was not toxic. All three compounds increased cellular reactive oxygen species (ROS) concentration-dependently, with a further increase by Fe^{2+} or hemin. Mice treated orally with up to 800 mg OZ78, or MT04 showed no relevant hepatotoxicity. In conclusion, we confirmed fasciocidal activity of OZ78 and MT04, which was increased by Fe^{2+} or hemin. OZ78 and MT04 were toxic to HepG2 cells, which was explained by mitochondrial damage associated with ROS generation in the presence of iron. No relevant hepatotoxicity was observed in mice in vivo, possibly due to limited exposure and/or high antioxidative hepatic capacity.

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Distinct processing of tone offset in two primary auditory cortices

Magdalena Sołyga & Tania Rinaldi Barkat

Abstract

In the rodent auditory system, the primary cortex is subdivided into two regions, both receiving direct inputs from the auditory thalamus: the primary auditory cortex (A1) and the anterior auditory field (AAF). Although neurons in the two regions display different response properties, like response latency, firing threshold or tuning bandwidth, it is still not clear whether they process sound in a distinct way. Using *in vivo* electrophysiological recordings in the mouse auditory cortex, we found that AAF neurons have significantly stronger responses to tone offset than A1 neurons. AAF neurons also display faster and more transient responses than A1 neurons. Additionally, offset responses in AAF – unlike in A1, increase with sound duration. Local field potential (LFP) and laminar analyses suggest that the differences in sound responses between these two primary cortices are both of subcortical and intracortical origin. These results emphasize the potentially critical role of AAF for temporal processing. Our study reveals a distinct role of two primary auditory cortices in tone processing and highlights the complexity of sound encoding at the cortical level.

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Above you can find the abstracts of recent articles published by members of the DBM. The abstracts are grouped according to the impact factor of the journal where the work appeared. To be included, the papers must meet the following criteria:

1. The first author, last author or corresponding author (at least one of them) is a member of the DBM.
2. Department of Biomedicine and University of Basel affiliation must be mentioned in authors list as published by the journal.
3. The final version of the article must be available (online pre-publications will be included when the correct volume, page numbers etc. becomes available).

We are focussing on original publications. Due to page constraints, abstracts of publications that appeared in lower ranked journals may not be able to be included. Review articles are generally not considered, unless they appeared in the very top journals (e.g. Cell, Science, Nature, NEJM, etc.). The final decision concerning inclusion of an abstract will be made by the chair of the Department of Biomedicine.

If you wish that your article will appear in the next issue of DBM Facts please submit a pdf file to the Departmental Assistant, Manuela Bernasconi: manuela.bernasconi@unibas.ch

Deadline for the next issue is February 29, 2020.

Merry Christmas

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Congratulations

Alessio Elia Campo Müller
Geboren am 14. Oktober 2019

Herzlich willkommen, allerseits!

IT'S CHRISTMAS IN ACCRA!!!

The clock is ticking, the atmosphere is saturated with excitement, cars honking at each other to make way through the heavy traffic, routes for commuters become overly choked with people, people walking at a fast pace, street hawkers in active business and seriously making huge sales, giant speakers squealing songs that have been hits during the year.... whew! It's almost like the population of the city doubled overnight.....it's the eve of Christmas in the capital, Accra, and this is exactly how the city comes alive throughout the most celebrated festive season in Ghana.

Many people travel to visit their families and friends in other parts of the country while people from the villages also get the opportunity to visit major cities. In local schools, it's common to find children making paper ornaments from crepe paper, children with artistic abilities tend to lead with unique decorations. Children present nativity plays or other festive drama during church services. It's also common to find the attendees singing traditional Christmas carols late into the night. There are usually street or beach carnivals at different locations within the city led by local musicians on Christmas Eve.

busy city

hotel decorated for Christmas

Christmas in Ghana is usually celebrated from the 20th of December and lasts through to the first week of the first month of the new year. With a population of about 28 million, the majority of Ghanaians, Christians (70%), celebrate Christmas whole heartedly. Although it is regarded as a Christian festival, it is enjoyed by all. December is also the start of the cocoa harvest (Ghana is the world's second biggest cocoa producer) and this coincides with the religious festivities, adding to the country's festive atmosphere. The common greeting to wish people a merry Christmas is "Afehyia Pa" (pronounced as Afishia pa) in Akan (the major ethnic language) which translates to "Merry Christmas and Happy New Year", and it is responded with same "Afehyia Pa"!

Pubs and bars also invite groups to perform live band music; patrons are treated to highlife, hiplife and dancehall genres. One cannot be idling at such events, people dance and drink to have great moments with friends. Masqueraders also dress up in their fanciful and colourful costumes and make these events more exciting…

carnival

On Christmas day, the churches are filled to capacity. People dress up in colourful clothes, different carols are sang throughout the church service. Afterward, young children receive chocolates, cookies or new clothes from Father Christmas before heading home for one more massive festive meal. Families and friends also gather around to feast on special foods prepared for the season. Jollof rice (check recipe), chicken, goat, waakye (rice & beans with spicy black chilli sauce called 'shito'), fufu, etc. Fufu is a staple food found in Ghana and is made from pounding and mixing cassava and plantain into a homogenous paste, enjoyed with different soups.

Christmas is a season of love and a season of gifts! It is not uncommon to see people give gifts to friends and family just as everywhere else around the world. It's also a season for sharing chocolates as gifts especially on boxing day. The children in Ghana see Father Christmas, or "Papa Bronya", as someone who wears sandals and a beautiful red robe trimmed in a golden fabric. His outfit is

Recipe for Ghanaian Jollof rice

Jollof (jol-ôf) rice is a special and popular dish that is enjoyed by all Ghanaians. Jollof has many variations; it could be made with meat, vegetables, or tofu. The uniquely orange-coloured rice is often the major dish at almost every event, parties, weddings, and Christmas.

Ingredients (for 5 servings)

- 6 oz tomato paste (170 g), 1 can
- 14 oz diced tomato (395 g), 2 cans
- ⅓ cup vegetable oil (80 mL)
- 1 habanero pepper
- 2 teaspoons curry powder
- 1 teaspoon garlic powder
- 3 chicken bouillon cubes, crushed
- 2 ½ cups long grain rice (500 g)
- 1 cup frozen mixed vegetable (150 g)
- 1 ½ cups water (360 mL)
- 2 large yellow onions, roughly chopped
- 1 teaspoon ground ginger
- ½ teaspoon mixed dried herbs
- 2 medium onions blended with 1 teaspoon ground ginger, ½ teaspoon mixed dried herbs and 2 cloves of garlic (to steam meat)
- 3 lbs chopped meat (turkey/pork/lamb, etc)

Preparation

- Put the chopped meat into a pot and add the blended ginger, onion, garlic and herbs.
- Add ⅓ cup of water, a pinch of salt, mix and steam over high heat for 10 – 15 mins with occasional stirring. Place aside when cooked.
- Add onions and 2 tablespoons of oil to a blender and pulse until smooth. Transfer to a medium bowl.
- Add the diced tomatoes, tomato paste, and habanero pepper to the blender, and pulse until smooth. Transfer to a separate medium bowl.
- Heat the remaining ⅓ cup (80 ml) of oil in a large, heavy-bottomed pot over medium heat.
- Once the oil is simmering, add the onion puree and cook until the water has cooked out and the puree is starting to brown, about 10 minutes.
- Stir in the tomato puree and add the curry powder, garlic powder, ginger, dried herbs, and crushed bouillon

complete with a traditional African patterned sash and a white cloak with a hood. While Christmas trees are popular in Western culture, they are not a common sight in homes in Ghana. The locals would rather spend their money on more food for the Christmas feasts than on a Christmas tree. Usually, decorated trees are found in shopping malls, companies or hotels. Otherwise, you might find a community tree in the centre of the town. It will be decorated with colourful paper ornaments that children create for their homes and schools. One amazing thing is even if some families don't have the means for regular meals, neighbours and friends will invite each other around to join in on a set buffet, throughout the two-week celebrations in December.

It is definitely worthwhile to travel to Ghana and have a taste of how Christmas is enjoyed. You can't miss the rich music, culture and amazingly hospitable Ghanaians no matter their ethnic background.

Frederick Bright

cubes. Cook for 20-30 minutes, stirring occasionally, until the stew has reduced by half and is deep red in colour.

› Add the steamed meat and allow to simmer for 5 minutes.

› Add the rice, mixed vegetables, and water. Bring to a boil, then reduce the heat to low and cover the pot with foil and a lid. Simmer for another 30 minutes, until the rice is cooked through and the liquid is absorbed.

› Jollof is ready and could be enjoyed with salads, fried plantain or other side dishes…

Enjoy!

Sag es mit positiver Psychologie

Radek Skoda hat es im Editorial schon angesprochen. Wir alle freuen uns über ein ernst gemeintes Kompliment. Auch die Forschung zeigt, dass das Sehen von Charakterstärken seitens unserer Mitmenschen einen grossen Einfluss auf unser Wohlbefinden hat. Doch es ist nicht immer einfach, die richtigen Worte zu finden. Die Elevation Cards bieten hier Abhilfe. Mit ihnen kann man Stärken mitteilen und miteinander teilen (siehe Bild). Auf der Rückseite kann man sogar noch eine entsprechende Situation vermerken. Zur jeweiligen Charakterstärke gibt es auch noch eine kurze Erklärung. Die Kärtchen sind ab Januar 2020 im Bereichssekretariat im 2. Stock ausgelegt. Wer Lust hat, macht mit. Viel Freude dabei!

Say it with positive psychology

Radek Skoda has already mentioned it in the editorial. We all enjoy an honest compliment. Research also shows that seeing character strengths on the part of our fellow human beings has a great influence on our well-being. But it is not always easy to find the right words. The Elevation Cards offer a remedy here. They can be used to communicate and share strengths (see below). On the back you can even note a corresponding situation. There is also a short explanation of each character strength. The cards will be available from January 2020 on in the secretariat on the 2nd floor. Join in, if you feel like it. Have fun with it!

Heidi Hoyermann

Help Santa find his reindeer

Merry Christmas

Linus Peter neuer IT-Lehrling

Seit kurzem habe ich das DBM-IT Team kennengelernt und konnte mich mittlerweile schon gut integrieren.

Die Lehre als Systemtechniker EFZ im Universitätsspital hat mir sehr zugesagt. Umso mehr habe ich mich über die Zusage vom Universitätsspital gefreut. Es war auch ein gewisser Stolz dabei, da meine Sekundarstufenlehrerin mir nicht gerade grosse Hoffnungen in puncto Lehrstelle als Informatiker in Basel gemacht hat. Denn laut ihr würden alle Betriebe, welche Lehrstellen für Informatiker anbieten, natürlich P-Zug Schüler bevorzugen. Was glücklicherweise für mich als E-Zug Schüler ja nicht ganz gestimmt hat.

Hier im DBM bin ich sehr gerne und fühle mich wohl. Aber ausserhalb des DBM verbringe ich auch sehr gerne Zeit ohne Computer. Unter anderem mag ich Tiere. Früher hatte ich nacheinander verschiedene Haustiere wie Kaninchen oder Mäuse. Der Vorteil an diesen Tieren ist, dass sie pflegeleicht sind. Morgens die Kaninchen raus ins Aussengehege lassen, am Abend wieder rein und mindestens einmal in der Woche das Gehege säubern. Dies lässt sich neben der Schule oder Ausbildung leicht einrichten. Aber ein Hund hingegen braucht sehr viel Zuneigung und ist zeitaufwendig zu halten. Und da ich schon seit Längerem einen Hund haben möchte, aber es aus den eben genannten Gründen für mich unmöglich ist, einen zu halten, gehe ich regelmässig mit den Hunden aus dem Tierheim raus. Für mich ist dies die perfekte Lösung, da ich, wenn ich keine Zeit habe, keinen Hund alleine zuhause lasse.

Natürlich verbringe ich auch viel Zeit damit, Videospiele zu spielen, wie die meisten Jugendlichen in meinem Alter. Neben den Spielern gibt es aber auch noch die Seite, welche die Spiele entwickeln muss. Seit kurzer Zeit lernen ein paar Freunde und ich auch die andere Seite kennen. In einer Gruppe, bestehend aus vier Personen, haben wir ein ziemlich grosses Projekt gestartet. Wir haben angefangen unser eigenes Spiel zu entwickeln. Seit etwa einem Monat arbeiten wir uns in die Spielentwicklungsmaterie ein. Dies braucht natürlich seine Zeit, da so ein grosses Spiel nicht nur aus einem Programm entstehen kann. Es benötigt 3D-Programme, um die Objekte zu formen, Audio Programme, um die Musik zu komponieren, Animationsprogramme, um Bewegungen zu erstellen, und schlussendlich noch eine Engine, in der alles zu einem Spiel zusammengefügt wird. Dies klingt jetzt vielleicht nach sehr viel Arbeit, was es natürlich auch ist. Deshalb fangen wir einfach mal an und schauen, wie weit wir kommen. Ziel ist es aber, die einzelnen Programme zu kennen und zukünftig, falls noch Bedarf vorhanden ist, andere Spiele zu entwickeln.

Wie Silvester in unterschiedlichen Ländern gefeiert wird

Silvester wird zwar weltweit in fast allen Ländern jeweils am Abend des 31. Dezembers gefeiert, aber jedes Land hat dafür andere Traditionen, Rituale oder Bräuche.

Silvester in Italien
Hier ist rote Unterwäsche in der Neujahrsnacht ein absolutes Muss. Wer glücklich und erfolgreich sein möchte, sollte mit roter Wäsche ins neue Jahr «rutschen». Kaufhäuser und Dessous-Läden stellen daher jedes Jahr spätestens kurz nach Weihnachten ihre Wäscheauslage um. Egal ob Spitzenhöschen oder Boxershorts – Hauptsache rot. Zu essen gibt es traditionell Schweinshaxe mit Linsen. Die deftige Kost bringt angeblich Glück in Gelddingen.

Silvester in Frankreich
Wer den Jahreswechsel in Frankreich verbringt, darf keine ausgelassenen Feiern oder buntes Feuerwerk erwarten. In den meisten Orten des Landes geht es in der Silvesternacht relativ ruhig zu. Viele Franzosen treffen sich lediglich mit Freunden und Verwandten zum Abendessen. Statt mit Böllern und Raketen wird das neue Jahr gewöhnlich kulinarisch mit Champagner, Stopfleber (Foie gras) oder Austern begrüsst. In Städten wie Paris ist die Böllerei sogar ganz untersagt. Die grösste Silvesterparty steigt in der Regel auf der Pariser Prachtstrasse Champs-Elysées. Dort feiern um Mitternacht Hunderttausende und wünschen sich «Bonne année» (Gutes Jahr).

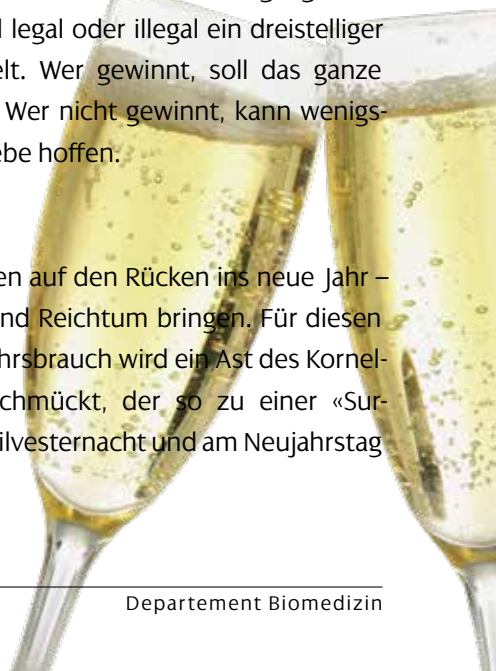
Silvester in Spanien
Hier gehören unbedingt Weintrauben zur Neujahrsnacht, die Glück bringen sollen. Um Mitternacht schieben sich viele Spanier bei jedem Glockenschlag eine Traube in den Mund. Wer sich verzählt, dem steht im neuen Jahr Unheil bevor. Supermärkte bieten für die Silvesternacht eigens Konservendöschen mit zwölf Trauben an. In den Kneipenvierteln der Städte verkaufen fliegende Händler kurz vor zwölf Plastiktütchen mit zwölf Weintrauben – dann oft zu Wucherpreisen.

Silvester in Tschechien
Hier giessen viele Familien Blei, um in die Zukunft zu schauen – noch älter aber ist der Brauch, einen Apfel zu halbieren und am Kerngehäuse das Schicksal abzulesen. Bilden die Kerne ein Kreuz, droht Unheil; in Sternform stehen sie für Glück. Finanziellen Erfolg soll nach tschechischer Tradition ein Mitternachtsessen mit Linsen bringen, die Geld symbolisieren. Die Hauptstadt Prag organisiert seit den 90er Jahren am Abend des 1. Januar stets ein grosses Feuerwerk, das Zehntausende anlockt.

Silvester in Grossbritannien
Hier zündet an Silvester kaum jemand ein Feuerwerk – richtig geschossen wird im Königreich bereits am 5. November, dem Tag, an dem der Offizier Guy Fawkes ein Attentat auf König Jakob I. versuchte. Organisierte Feuerwerke gibt es zu Silvester jedoch auch in Grossbritannien. Das wohl grösste steigt am Londoner Riesenrad «London Eye». Dort versammeln sich Jahr für Jahr hunderttausende Menschen, um das pompöse Lichterspiel zu bestaunen. Das Spektakel wird auch live im Fernsehen übertragen.

Silvester in Griechenland
Zum Neujahrsfest wird hier gezockt. Es geht hoch her bei Karten- oder Würfelspielen zu Hause oder im Kasino. Das grosse Neujahrszocken beginnt bereits am Abend des 31. Dezember und dauert oft bis zum Sonnenaufgang am 1. Januar. Landesweit wird legal oder illegal ein dreistelliger Millionenbetrag verspielt. Wer gewinnt, soll das ganze Jahr über Glück haben. Wer nicht gewinnt, kann wenigstens auf Glück in der Liebe hoffen.

Silvester in Bulgarien
Hier geht es mit Schlägen auf den Rücken ins neue Jahr – sie sollen Gesundheit und Reichtum bringen. Für diesen weit verbreiteten Neujahrsbrauch wird ein Ast des Kornelkirschbaums bunt geschmückt, der so zu einer «Surwatschka» wird. In der Silvesternacht und am Neujahrstag



gehen Kinder von Haus zu Haus und schlagen damit die Bewohner auf den Rücken. Dabei wünschen sie nach alter Tradition ein gesundes, glückliches, fruchtbares und reiches neues Jahr. Dafür bekommen sie kleine Geschenke wie Bonbons, Kuchen, Früchte oder Kleingeld.

Silvester in den USA

Vor allem im Süden der USA werden zu Silvester gerne Linsen oder Linsensuppe gegessen. Weil die Linsen ein bisschen wie Münzen aussehen, sollen sie Glück und Geldsegen versprechen. In Teilen Pennsylvanias - dort, wo früher viele Deutsche siedelten – gehört auch Sauerkraut zu den Traditionsgerichten. Dann gibt es noch die Regel «Nothing Goes Out», nach der am ersten Tag des Jahres nichts das Haus verlassen darf, auch nicht der Müll. Wenn doch, droht Unglück.

Silvester in Argentinien

Hier, auf der Südhalbkugel, treffen sich die meisten Menschen bei hochsommerlichen Temperaturen am frühen Abend mit Freunden und kochen, essen und reden bis Mitternacht. Um Punkt 0.00 Uhr bricht ein atemberaubendes Feuerwerk los. Tausende Menschen stehen auf den Flachdächern ihrer Häuser, um das Spektakel besser sehen zu können. Zu gutem heimischem Sekt heisst es dann «Feliz Año Nuevo!» (Frohes Neues Jahr!). Wer Lust hat, kann sich dann ab etwa 2.00 Uhr morgens in Clubs und Bars vergnügen. Aber Vorsicht: Schon von 8.00 Uhr an brennt einem die Sonne gnadenlos auf den verkaterten Kopf.

Silvester in Russland

Die für rauschende Partys bekannten Russen läuten mit dem letzten Tag des Jahres eine zehntägige Festphase ein. In der Neujahrsnacht bringen Väterchen Frost, das Pendant zum Weihnachtsmann, und seine Begleiterin Snegurotschka (Schneeflöckchen) die Geschenke. Im ganzen Land werden Jolka-Feste gefeiert. Gemeinsam sitzt die Familie um die Jolka (den Tannenbaum) herum und isst. Nachdem die Präsidentenrede im Fernsehen vorbei ist, wird auf das neue Jahr angestossen. Die russisch-orthodoxe Kirche richtet sich anders als die westlichen Kirchen nicht nach dem Gregorianischen, sondern nach dem Julianischen Kalender: Weihnachten wird erst in der Nacht zum 7. Januar gefeiert, Neujahr ist erst am 13. Januar.

Silvester in China

Die Chinesen begehen Silvester eher ruhig mit einem Abendessen im Kreise der Familie oder mit Freunden. Feuerwerk gibt es nicht. Umso grösser wird dafür das chinesische Neujahrsfest nach dem traditionellen Mondkalender gefeiert, das 2020 auf Ende januar fällt. Dann kommt das Milliardenreich für mindestens eine Woche praktisch zum Stillstand. In einer Völkerwanderung reisen viele Millionen Chinesen in ihre Heimatdörfer. Am Vorabend des Neujahrsfestes, das auch Frühlingsfest genannt wird, werden traditionell kleine Teigtaschen gegessen, deren Form an alte chinesische Geldstücke erinnert und deswegen Glück und Reichtum verheissen soll. Den ganzen Abend wird Feuerwerk gezündet.

« Weihnachten – Nächte, die Tage sind. »

Eberhard Horst Bellermann