Schweizerische Gesellschaft für Klinische Chemie
Société Suisse de Chimie Clinique
Società Svizzera Chimica Clinica
Swiss Society of Clinical Chemistry

SSCC 2025

Annual Assembly

26th August 2025, 9 am - 6 pm

Bern UniS – Schanzeneckstrasse 1 – 3012 Bern

Schweizerische Gesellschaft für Klinische Chemie
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Program

SSCC 2025 Annual Assembly
Tuesday, August 26th

From 8:30	**Registration with coffee and croissants**	
9:00	**Welcome words** (Pierre-Alain Binz, Déborah Mathis)	
9:05–10:55	**IVDR regulation: opportunities and challenges** Chair: Daniel Müller, Christoph Seger	
9:05	Requirements and challenges for in-house IVDs under IvDO/IVDR	**Dr. Damian Hertig**
9:40	The story behind IVDR/IvDO & impact on the industry and the Swiss healthcare system	**Bernhard Bichsel**
10:15	Implementation of the EU Regulation on In Vitro Diagnostic Medical Devices (IVDR): First experiences in Germany	**Prof. Dr. Michael Vogeser**
11:55–11:10	**Coffee break**	
11:10–12:20	**Selected talks from abstracts** Chair: Barbara Rindlisbacher, Laura Millius	
11:10	Pre-analytical considerations in the simultaneous quantification of ketone bodies, pyruvate, lactate, and TCA cycle intermediates	**Kaitlyn Berchier**
11:27	Design and assessment of a microsampling-based interlaboratory comparison for phosphatidylethanol analysis	**PD Dr. Marc Luginbühl**
11:45	Identifying whether the source is the tube or the stopper: Evaluation of zinc and antimony contamination in BD blood collection tubes	**Delia Faccioli**
12:02	SSCC Förderpreis presentation	**Dr. Henning Nilius**
12:20–13:30	**Lunch break with poster presentation**	

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13:30–14:15	**Annual assembly of the SSCC**	**Dr. Pierre-Alain Binz**
14:15–16:00	**Patient self-sampling and testing** Chair: Viola Günther, Joanna Gawinecka	
14:15	Advancing diabetes care: self-testing, sensor technology, and laboratory integration	**Prof. Dr. Lilian Witthauer**
14:50	Therapeutic drug monitoring of tacrolimus and mycophenolic acid in outpatient renal transplant recipients using a volumetric dried blood spot sampling device.	**Prof. Dr. D.J.A.R. Moes**
15:25	Cutting-edge innovations in self-testing	**Dr. Markus Schmid**
16:00–16:15	**Coffee break**	
16:15–17:30	**Healthy aging and self-optimization: what to test?** Chair: Philipp Walter, Déborah Mathis	
16:20	DNA methylation as biomarker for aging	**Prof. Dr. Ursula Amstutz**
16:55	Clinical reasoning in micronutrients testing	**PD Dr. Stefan Markun**
17:30	**Closing words with poster price** (Carlo Largiadèr)	
From 17:35	**Apéro**	

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Presenting Author: Kaitlyn Berchier

Kaitlyn Berchier[1,2], Chiara Nyffeler[1], Stephen Bruce[3], Clothilde Roux[3], Jean-Marc Nuoffer[1,4], Matthias Gautschi[1,4], Alexander Lämmle[1,4], Déborah Mathis[1*]

Pre-analytical considerations in the simultaneous quantification of ketone bodies, pyruvate, lactate, and TCA cycle intermediates

Introduction

Accurate quantification of small metabolites such as ketone bodies (KB: β-hydroxybutyrate [BHB], acetoacetate [AcAc]), pyruvate (Pyr), lactate (Lac), and tricarboxylic acid (TCA) cycle intermediates is essential for clinical diagnostics and metabolic research. These metabolites serve as energy substrates and signaling molecules, with interpretation often relying on physiologically meaningful ratios (e.g., Lac/Pyr, AcAc/BHB). However, their chemical lability and susceptibility to rapid post-collection metabolic changes pose significant analytical challenges.

Methods

We developed an LC-MS method for simultaneous quantification of KB, Pyr, Lac, and TCA intermediates, and systematically evaluated pre-analytical factors affecting their stability and accuracy. We compared Li-heparin (LH), EDTA, sodium fluoride/EDTA (NaF), and sodium citrate (NaCit) collection tubes, as well as deproteinized whole blood (depWB) treated with perchloric acid.

Results

Stability was assessed in plasma at room temperature (RT) over 24 hours, and in LH and depWB at RT, 4 °C, and –20 °C over 7 days. Pyr, Lac, AcAc, and fumarate were most labile, while BHB and citrate remained stable. LH-plasma showed minimal metabolic changes and yielded consistent results. NaF effectively stabilized Lac but compromised Pyr and TCA intermediates. DepWB improved Lac/Pyr ratio reliability but introduced greater variability and matrix effects. NaCit induced unexpected metabolic shifts, suggesting in vitro TCA activity.

Conclusion

Pre-analytical variables critically impact metabolite integrity. LH-plasma offers the best compromise for routine quantification when processed rapidly. DepWB remains the method of choice for precise Lac/Pyr ratio determination, despite its increased variability.

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Presenting Author: Delia Faccioli

D. Faccioli[1], V. Gantenbein[1], C. Seger[1], N. Gibitz-Eisath[1]

Identifying whether the source is the tube or the stopper: Evaluation of zinc and antimony contamination in BD blood colleczion tubes

Introduction

In a previous study [1], various blood collection tubes were evaluated regarding their suitability for trace element quantitation. Elevated zinc (66Zn) and antimony (121Sb) levels were detected in certain blood collection tubes manufactured by Becton Dickinson (BD). These outcomes were hypothesized to be related to the tube components: most BD stoppers consist of butyl rubber, whose manufacturing process involves the use of zinc salts, while the tubes themselves are made of polyethylene terephthalate (PET), where antimony is used as a catalyst during fabrication. This study aimed to clarify this hypothesis by determining whether the source of contamination originated from the tube or the stopper.

Methods

Three representative tube types were included: a serum tube with gel (BD-RST, 368774), a heparin tube with mechanical barrier (BD-BC, 365049) and a serum trace element tube (BD-TE, 368380). Each type was analyzed in triplicate. Tubes were filled with 5 ml of 0.1 % HNO3 and stored upright until analyzed. Stoppers were incubated separately in Sarstedt screw-cap tubes (pre-tested to be contamination free) containing 15 ml of 0.1% HNO3. Zn and Sb were quantitated after 2, 6, 24, and 48 h of incubation using inductively coupled plasma mass spectrometry (ICP-MS, PerkinElmer, NexION 2000B under Recipe ClinCal Serum Trace Elements Calibration). Contaminations were considered as relevant if the measured concentration exceeded 25% of the lower limit of the reference range (Zn 0.180 mg/L) or the clinical cut-off (Sb 0.05 µg/L).

Results

Significant Sb contaminations (exceeding the defined cut-off by over 100-fold) were detected in the BD-RST and BD-TE tubes, whereas their stoppers showed no relevant Sb release. The BD-BC tube showed contamination in both tube and stopper, although concentrations were clearly lower than in the other two merchandises.

Clinically relevant Zn levels, which increased slightly with exposure time, were detected in the stoppers of both conventional tubes (BD-RST and BD-BC). No relevant contamination was observed in either the tube or stopper of the trace element device (BD-TE).

Discussion and Conclusion

The findings support the hypothesis that Sb contamination originates primarily from the PET tube material, as also noted by the manufacturer. The stoppers are identified as the source of the observed Zn-contamination in conventional devices. However, the study design involved certain limitations: HNO3 was used as a surrogate matrix instead of serum, and the stoppers were fully immersed rather than exposed to a brief contact typical in clinical blood draws. Although the experimental setup simulates a worst-case scenario, the findings nonetheless indicates that a clinically relevant influence remains a realistic concern.

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Presenting Author: Nicholas Küng

Nicholas Kueng[1,2], Fanny Sandberg[1,2], Daniel Sidler[3], Vanessa Banz[4], Annalisa Berzigotti[5], Charlotte K.Y. Ng[6,7], Carlo R. Largiadèr[1], Ursula Amstzutz[1*]

Mapping Cell-Free DNA Tissue Origin in Transplant Recipients Through Methylation Signatures

Introduction

Donor-derived cell-free DNA (dd-cfDNA) is a valuable biomarker for solid organ transplant monitoring but has some limitations. Tissue-specific DNA methylation offers an alternative approach to identify cfDNA tissue origins without relying on donor-recipient genotype differences. Here, we present a targeted sequencing assay to determine cfDNA tissue of origin (TOO) and dd-cfDNA proportion, addressing limitations in transplant monitoring and advancing patient care.

Methods

Utilizing a methylation atlas of 40 human cell types, we developed a targeted capture panel for deep methylation sequencing of cfDNA. cfDNA was extracted from plasma of kidney (KT) and liver recipients (LT), as well as healthy controls (HC), and subjected to targeted methylation sequencing to determine the cfDNA TOO in genome equivalents/mL (GE/mL).

Results

Genomic DNA analysis showed 93-98% accuracy for kidney epithelium, hepatocytes, B- and T-cells with detection sensitivity as low as 0.3%. Mean cfDNA from kidney epithelium was higher in stable LT (n=20, 31 GE/mL) and KT (n=31, 29 GE/mL) recipients compared to HC (n=23: <1 GE/mL). Hepatocyte cfDNA was similarly elevated (LT: 147; KT: 107; HC: 48 GE/mL). KT exhibited increased megakaryocyte cfDNA compared to LT or HC. Within 24 hours post-transplantation, only a minority (median: 5%, interquartile range, IQR: 0-12%) of ddcfDNA in KT (n=18) originated from the kidney epithelium, while a median of 82% (IQR: 60-96%) originated from hepatocytes in LT (n=15). The remaining dd-cfDNA was predominantly of hematological and endothelial in origin.

Conclusion

We developed a targeted deep methylation sequencing workflow that allows accurate TOO deconvolution of cfDNA from a single standard blood collection tube. This enables precise monitoring of organspecific injury in transplantation, potentially improving the management of transplant recipients, as indicated by distinct tissue injury profiles.

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Presenting Author: Marc Luginbühl

Matthias Bantle[1], Frederike Stöth[1,2], Wolfgang Weinmann[1], Marc Luginbühl[2,3]

Design and assessment of a microsampling-based interlaboratory comparison for phosphatidylethanol analysis

Introduction

Phosphatidylethanol (PEth) has become a widely recognized and reliable biomarker for assessing alcohol consumption and monitoring abstinence. Its increasing use in clinical and forensic contexts underscores its significance in evaluating drinking behavior. However, despite its growing adoption, there remains a lack of comprehensive knowledge regarding the robustness, standardization, and comparability of methodologies and results across laboratories. Recognizing this gap, the first international consensus on the use and interpretation of PEth was published in 2022, providing a foundational framework for harmonizing its application.

Methods

To further this effort, an interlaboratory comparison study involving three rounds of testing with microsamples was conducted. The study aimed to establish an experience-based foundation for standardization and method harmonization. Participating laboratories provided their sampling devices, which were subsequently sent to the Forensic Toxicology Laboratory at the University of Bern. For each round, four authentic blood samples with predetermined PEth concentrations were applied to the devices and returned to the laboratories for analysis.

The target concentrations of PEth 16:0/18:1, the most commonly measured homologue, ranged from 16 to 474 ng/mL (0.023–0.676 µmol/L). These values included concentrations close to critical decision thresholds of 20 ng/mL (0.025 µmol/L) and 200 ng/mL (0.28 µmol/L), which are relevant for differentiating social drinking, excessive consumption, and abstinence.

Results

The results were evaluated according to guidelines established by Horwitz and the Society of Toxicological and Forensic Chemistry (GTFCh). Among the participating laboratories, 73% successfully quantified and reported all four samples within acceptable limits for each round. Furthermore, over 90% of laboratories quantified and reported at least one sample within acceptable limits, demonstrating a high level of analytical capability overall.

Conclusion

This study highlights the feasibility of interlaboratory comparisons using microsamples and underscores the need for continued efforts to harmonize methods and enhance reliability. These findings contribute to the development of standardized protocols and foster greater confidence in the use of PEth as a biomarker for alcohol consumption.

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Presenting Author: Selina Mazenauer

S. Mazenauer[1], P. Neyer[1], L. Bernasconi[1]

Calculating albumin-adjusted calcium: the advantage of using a locally derived formula

Background
Deviations in circulating calcium levels occur in various pathological conditions, including skeletal, (para)thyroid, and kidney diseases. Approximately half of total serum calcium is bound to albumin, while the remaining half circulates in its ionized form, which is biologically active. Variations in albumin levels thus influence the concentrations of total serum calcium, while ionized calcium levels remain constant. However, total serum calcium is routinely measured instead of ionized calcium, primarily for practical reasons. To account for deviations in albumin levels, albumin-adjusted total calcium levels are commonly reported as an alternative to direct ionized calcium measurement.

Aim
Various formulas exist for adjusting total calcium levels. We highlight the advantages of a locally derived, internally validated albumin-adjusted calcium equation compared to relying solely on total serum calcium measurements or rigid historical correction formulas that do not consider nor the local sample collective nor analytical techniques.

Methods
Albumin-adjusted total calcium levels were calculated with a locally derived formula developed as described by James et al. based on data of 3694 patients. The correlation between unadjusted and albumin-adjusted total calcium levels with ionized calcium levels was then assessed.

Results
The locally derived formula for albumin-adjusted calcium provided a more accurate assessment of calcium status compared to measuring total calcium alone or using previously established, fixed correction formulas.

Conclusion
Our results demonstrate the feasibility of developing and using a locally derived formula for albumin-adjusted calcium correction. The locally adjusted formula provides a surrogate marker for ionised calcium and outperforms both the sole assessment of unadjusted total calcium and the simplified Payne formula for adjusted total calcium.

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Presenting Author: Henning Nilius

Henning Nilius *[1] , Michael Stickel* [1] , Karin Volken [1], Alex Tolkmitt [1], Michael Nagler [1] , for the EPIC-Beaker implementation group

A next-generation integrated Laboratory Information System: Experience from the first Epic-Beaker implementation in Switzerland

Background

Traditional laboratory information systems (LIS) operate as stand-alone solutions, with an essentially one-way flow of information from the laboratory to the electronic health record (EHR) system. Consequently, laboratories have been treated as external service providers, which has limited the opportunities for innovation in healthcare processes.

Methods

At Inselspital, Insel Gruppe AG, we implemented the EHR system Epic (Epic Systems, Verona, Wisconsin, USA) in March 2024. In response, the center of laboratory medicine decided to switch to its integrated LIS module 'Beaker'. Beaker is an inherent part of the EHR, which means that the EHR and the LIS use a unified database. Here, we report on key insights from the first Beaker implementation in a German-speaking university hospital.

Results

Within two years of preparation, we formed an interdisciplinary team with a shared vision, uniting IT, EPIC experts, laboratory professionals, and clinical stakeholders. Key success factors included giving the teams the authority to decide (empowerment), recruiting analysts with laboratory expertise, and conducting extensive system testing. Four examples illustrate the apparent advantages:

First, Epic enables closed-loop sample tracking from blood draw to storage, recording time, user, and location. While this required adjustments in nursing routines, it has reduced identification errors, achieved full traceability, and essentially eliminated manual search.

Second, up-to-date and full clinical information is directly accessible within the lab user interface, supporting safe validation and active communication with clinical teams.

Third, the unified database links lab results with clinical data such as diagnoses, allowing real-time monitoring of key performance metrics such as device performance, turnaround times, and test utilization, while also supporting targeted research projects.

Fourth, the technical flexibility of the system also enabled the successful implementation of an in-house diagnostic decision-support machine learning model.

Challenges included adapting to differences in laboratory traditions between Switzerland and the US. For example, custom PDF reporting capabilities are very limited.

Conclusion

An integrated LIS, like EPIC-Beaker, has the potential to transform the laboratory's role from a passive result provider to an active partner in clinical care and research, thus supporting patient safety, operational efficiency, and diagnostic innovation.

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An accurate and pragmatic diagnostic algorithm for heparin-induced thrombocytopenia (HIT) in critically ill patients: an analysis of the TORADI-HIT study

Introduction

Diagnostic tools and scoring systems that have not been specifically validated in the context of critical illness are mostly not useful for ICU staff. This also applies to tests for heparin-induced thrombocytopenia (HIT). We thus aimed to validate an accurate and pragmatic machine-learning (ML) algorithm integrating both clinical data and laboratory tests to predict the presence of HIT.

Methods

For this analysis, we included mixed surgical-medical ICU patients from the prospective multicenter TORADI-HIT cohort. TORADI-HIT enrolled patients with suspected HIT (defined by either anti-heparin/PF4 immunoassay ordered or application of the 4Ts Score) across 10 study centers in Switzerland, Germany, and the United States. Clinical and laboratory data were collected, and multiple anti-heparin/PF4 immunoassays were performed. HIT was defined by a positive heparin-induced platelet activation (HIPA) assay, which is considered the reference gold standard. We investigated the diagnostic performance of the TORADI-HIT algorithm and current diagnostic tests (including the American Society of Hematology (ASH) algorithm) alongside clinical outcomes.

Results

Of 519 ICU patients, 473 (91.1%) had complete data and were analyzed. HIT was confirmed in 7.8% of cases (n = 37); the median age was 66 years (62.6% male). Sepsis was present in 327 patients (69.1%), 73 (15.4%) had an intra-arterial device, and 96 (20.3%) had undergone major surgery. The area under the receiver operating characteristics curve of the TORADI-HIT algorithm for the presence of HIT was 0.97 (95% CI: 0.94, 1.00) (false negative rate 8.1%, (FNR) with a false-positive rate of 6.9% (FPR) n=30). In contrast, the ASH algorithm had a false-negative rate (FNR) of 13.5% (n = 5) and a false-positive rate (FPR) of 9.2% (n = 40). Patients with HIT developed venous thrombosis significantly more often than those without HIT (36.1% vs. 9.4%, $p < 0.001$).

Conclusion

Our data indicate that the TORADI-HIT algorithm is an accurate and pragmatic algorithm in the ICU population. It may contribute to reducing delayed HIT diagnosis and overtreatment in the critically ill.

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Presenting Author: Fanny Sandberg

F. Sandber[1, 2], N. Küng[1, 2], V. Banz[3], A. Berzigotti[3], C.R. Largiadèr[2], D. Sidler[4], U. Amstutz[2]

Inter- and intra-individual variability of donor-derived cell-free DNA in stable kidney and liver transplant recipients

Background

Donor-derived cell-free DNA (dd-cfDNA) is emerging as a non-invasive biomarker in kidney (KTx) and liver (OLT) transplant recipients for monitoring allograft health. Many studies have shown correlations between elevated dd-cfDNA fractions and graft rejections, potentially enabling earlier detection and treatment of graft dysfunctions. Our aim was to identify the inter- and intra-individual variability of dd-cfDNA in stable KTx and OLT within the first year after transplantation to determine baseline values and compare variability between absolute and relative dd-cfDNA quantification.

Methods

Blood and urine samples from KTx and OLT were collected longitudinally at regular visits. Mismatched HLA alleles between donor and recipient were used to determine absolute (cp/mL) and relative (%dd-cfDNA) quantities of dd-cfDNA using droplet digital PCR at three time points per recipient. Urinary dd-cfDNA was corrected for urine concentration using urinary creatinine (UCreat).

Results

The timepoints were not significantly different for any of the dd-cfDNA quantities of stable recipients (Tbl.A). Absolute and fractional dd-cfDNA quantities correlated significantly in plasma samples from KTx (r=0.47, p<0.001) and OLT (r=0.76, p<0.001) but not in urine samples of KTx (r=0.18, p=0.229). No significant correlation was found between plasma and urine samples of KTx (absolute: r=0.21, p=0.178; relative: r=0.22, p=0.144). Intra-individual variability was higher in plasma samples from KTx compared to urinary values or OLT (Fig.A). Adjusting absolute urinary dd-cfDNA quantities with the UCreat reduced the inter-individual variability (Fig.A).

Conclusion

We observed no significant dynamic of dd-cfDNA in the first year after transplantation of stable KTx or OLT. The contributions of inter- and intra-individual variability to dd-cfDNA quantities varied between OLT and KTx, and between urine and plasma, requiring further investigation including comparison to dd-cfDNA of non-stable KTx and OLT.

Table A: dd-cfDNA results of stable KTx and OLT

			KTx	
Fluid	Sample timepoints (mean days post-transplantation)	Number of samples	Median dd-cfDNA cp/mL (IQR)	Median %dd-cfDNA (IQR)
Plasma	T1 (54 ± 22)	16	5.90 (7.44)	0.086 (0.131)
	T2 (175 ± 34)	16	5.90 (8.15)	0.118 (0.216)
	T3 (351 ± 27)	16	4.19 (4.96)	0.119 (0.195)
Fluid	Sample timepoints (mean days post-transplantation)	Number of samples	Median dd-cfDNA cp/mL (IQR)	Median dd-cfDNA cp/mL corr. UCreat (IQR)	Median %dd-cfDNA (IQR)
Urine	T1 (54 ± 22)	14	248 (524)	47.5 (42.0)	17.5 (67.2)
	T2 (172 ± 33)	15	134 (522)	40.4 (76.1)	12.3 (41.6)
	T3 (351 ± 28)	15	70.3 (337)	19.8 (25.0)	11.6 (62.2)
			OLT	
Fluid	Sample timepoints (mean days post-transplantation)	Number of samples	Median dd-cfDNA cp/mL (IQR)	Median %dd-cfDNA (IQR)
Plasma	T1 (64 ± 22)	11	95.5 (78.7)	1.98 (1.57)
	T2 (154 ± 29)	11	135 (155)	0.926 (1.98)
	T3 (386 ± 74)	11	112 (139)	3.78 (7.31)

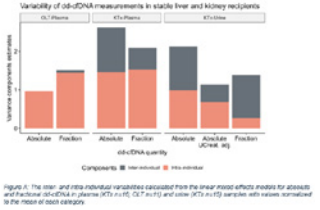

Figure A: The inter- and intra-individual variabilities calculated from the linear mixed effects models for absolute and fractional dd-cfDNA in plasma (KTx n=16, OLT n=11) and urine (KTx n=15) samples with values normalized to the mean of each category.

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Presenting Author: Marina I. Schläpfer

Marina I. Schläpfer[1, 3], Daniel Wegmann[2], Carlo R. Largiadèr[1]

Quantifying Genetic Effects on DPD Activity Using Bayesian Modeling of UH_2: U Ratios

Introduction

Fluoropyrimidines (FPs) such as 5-fluorouracil and capecitabine are cornerstone chemotherapies for solid tumors that are limited by the occurrence of severe toxicity in a subset of patients. The rate-limiting enzyme for FP catabolism is dihydropyrimidine dehydrogenase (DPD), encoded by DPYD, which degrades ~85% of administered drug. While several loss-of-function DPYD variants are clinically actionable, they explain only a small proportion of interindividual variability in toxicity risk.

Methods

To quantify the effects of DPYD variants and clinical covariates on DPD activity, a Bayesian hierarchical model was implemented using the R-package NIMBLE. The model estimated the posterior effects of established and candidate DPYD variants, age group, and sex on log-transformed plasma UH_2:U ratios in a Caucasian cohort. These ratios serve as validated surrogate markers of DPD enzymatic activity. Genotypes were modeled additively; age was modeled categorically. Markov Chain Monte Carlo sampling (30,000 iterations, 4 chains) achieved convergence ($\hat{R} < 1.1$), and posterior summaries were used to derive fold-changes and 95% credible intervals for each predictor. The model accounted for uncertainty in UH_2:U measurements through an estimated precision parameter (τ), mitigating the influence of intra-individual noise that could be from DPD circadian rhythm and having only one measurement per patient.

Results

As expected, known loss-of-function variants (DPYD c.1905+1G>A, c.1679T>G, c.2846A>T, and HapB3) were strongly associated with reduced DPD activity. Additional variants also showed potential effects; for example, c.85T>C has been associated with increased activity, while c.496A>G has been linked to decreased activity in prior studies. An age above 60 was associated with lower DPD activity, while sex had a minimal effect also consistent with current literature.

Conclusion

This Bayesian framework enables robust, probabilistic inference of genetic and demographic effects on DPD activity. It will serve as a foundation for integrating genome-wide association study findings to improve multivariable risk prediction and identify novel contributors to FP toxicity. Ultimately, this approach informs whether variant effects on DPD activity can be modeled at the population level and contributes to the advancement of genotype-guided dosing in oncology.

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Presenting Author: Christoph Seger

C. Seger[1], S. Niggli[1], S. Schwitzer[1], N. Gibitz-Eisatz[1]

Head-to-head comparison of two cystatin c assays

Introduction

Cystatin C (CysC) serves as serum-based marker for assessing the measured glomerular filtration rate (mGFR). It has advantages over creatinine-based mGFR, since it is independent from the muscle mass of the individual patient. With the introduction of a novel CysC assay format for the Abbott Alinity c platform (CysC_A) at our laboratory, a method comparison study was undertaken with the Roche Cobas c platform implementation (CysC_R).

Methods

Seventy samples from routine measurements (timeframe one month) performed with CysC_R (TinaQuant, ID 06600239 190), were evaluated in parallel with CysC_A (Sentinel, ID 06T32-30). According to the package inserts, both assays are traceable to ERM-DA471/IFCC. CysC based eGFR was calculated using gender- and age-adjusted CKD-EPI formulas [1], and statistical evaluation was performed after anonymization with MedCalc 20.019. KDIGO classification G1–G5 followed the AGLA [2].

Results

Pasing and Bablok regression analysis (CysC_A = 1.04*CysC_R – 0.12 mg/l) showed highly correlated data (Spearman's rho = 0.98 [95% CI 0.97-0.99]). Bland-Altman analysis revealed a +8.9% [95% CI 7.8-9.9%] method bias of CysC_A relative to CysC_R. CysC_A derived average eGFR was 8.8% [95% CI 7.8-9.8%] higher than CysC_R eGFR with a 2S-scatter range of ±8.5%. The CysC based CKD KDIGO classification showed class agreement with a Cohen's kappa of 0.86 [95% CI 0.77–0.95]. Classification differences were limited to G1 and G2, accounting for 78% of all cases. CysC_A led to 40 G1 and 15 G2 classifications, while CysC_R led to 29 G1 and 26 G2 classifications. Eleven cases classified as G2 with CysC_R changed to G1 with CysC_A.

Conclusion

The comparison of two IVD-CE-CysC assays performed under identical metrological traceability conditions revealed limited quantitative differences that are most likely not clinically significant. Since this investigation was limited in terms of space and time, it cannot be concluded that the average deviation of the inter-assay results found in this study represents a statistically sound systematic error contribution.

[1] Leseley A, Inker M.D., Christopher H, et al, Estimating Glomerular Filtration Rate from Serum Creatinine and Cystatin C. N Engl J Med 2012;367:20-29. [2] https://agla.ch/de/rechner-und-tools/niereninsuffizienz.

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Annual Assembly SSCC 2025 **Presenting Author: Jörg Oliver Thumfart**

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Examples for the use of QIP-MS (EXENT) in gammopathy disease management

Introduction

In gammopathy disease management (e.g., MGUS or multiple myeloma (MM)), the initial diagnosis often begins with a suspicious serum electrophoresis displaying an M-gradient, followed by immunofixation electrophoresis (IFE), quantification of the free light chains, and bone marrow puncture, which is then followed by sequencing or flow cytometry [1]. In the course of the therapy, this M-gradient should fade away, and the IFE should become inconspicuous. If complete remission is reached, one might look for MRD (minimal residual disease). In some cases, IFE remains positive for IgG-kappa despite a clinically successful therapy [2]. In such cases, the question arises whether this is a truly pathogenic clone (tumor product of an MM) or if this IFE signal is directed against a therapeutic monoclonal antibody (tmAB) [3].

Methods

Serum analysis for gammopathy patient follow-up. For patients from an oncology department, serum samples were analyzed by electrophoresis and IFE. For questionable results – MRD negative in the bone marrow and IFE positive – an attempt for clarification with QIP-MS (EXENT®) was tried. In the presented examples, these sera are tested for IgG, IgA, and IgM using Optilite with reagents from The Binding Site, allowing for quantitative analysis.

In addition, light chains kappa and lambda are analyzed with QIP-MS (EXENT®, The Binding Site).

Results

In both presented cases, we could clearly show the presence of a tmAB (Daratumumab). In one case, two clones were visible via QIP-MS. One displays the tmAB, and the other is (proofed by QIP-MS) the originally pathogenic tumor product.

Conclusion

We demonstrate the utility of the new QIP-MS technology for distinguishing tmAB from pathogenic tumor products in the management of myeloma disease. This capability will become increasingly important as the number of therapies using tmAB continues to increase exponentially. For this reason, the number of small gradients or slight bands visible by serum electrophoresis or IFE will also increase, and it is necessary to distinguish these therapy-related signals from true pathologies with unambiguous certainty.

For optimized patient care, we believe it is better not only to resolve unclear cases retrospectively with reserve samples (these will not always be available), but also to introduce EXENT® analysis as part of the characterization of a gammopathy in the long term.

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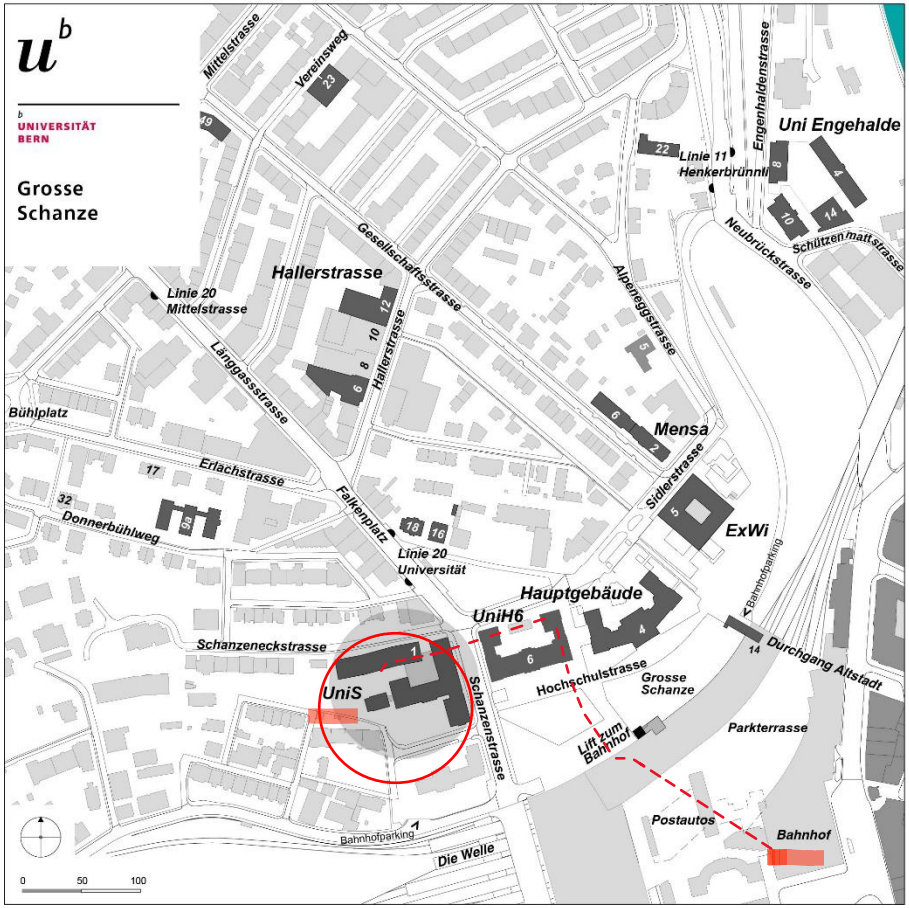

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