

# LEARNING WITHOUT BOUNDARIES

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## Department of Pathology & Molecular Medicine

### Laboratory Medicine Residency Training Programme Annual Residents' Research Day 2011

Thursday, May 12, 2011  
MDCL-3020 | 9:15 a.m.

**\* George Frank Memorial Lecture - MDCL-3020**

**"Controversies in the Diagnosis of Barrett's Esophagus and Barrett's-Related Dysplasia: One Pathologist's Perspective"** presented by:

**Dr. John R. Goldblum**, Chairman and Professor of Pathology, Cleveland Clinic Lerner College of Medicine. Case Western Reserve University. President of the Arthur Purdy Stout Society of Surgical Pathologists and Chair of the Education Committee for the United States and Canadian Academy of Pathology.

**\* Evening Lecture - The University Club**

**"Role and Implementation of Informatics"** presented by:

**Dr. Liron Pantanowitz**, UPMC Shadyside Hospital, Pittsburgh, PA., U.S.A.

#### MDCL & The University Club

R.S.V.P. by May 5, 2011  
to Laura McCarthy ext. 76900 or  
lmccar@mcmaster.ca

**Room locations:**

**Presentations - MDCL-3020**

**Posters - MDCL-3411 & 3412**

**\* Accredited Group Learning Activity**

in association with





## **Introductions**

The Laboratory Medicine Residents' Training Program would like to thank:

All the residents and fellows for their hard work and their contribution to the Residents' Research Day, as well as, the many supervisors supporting their work.

Thanks also to: Guest Speakers, Administration, Program Directors, and Laura Diskin for Programme support.

## **Guest Speakers**

### **George Frank Memorial Lecture**

#### **Controversies in the Diagnosis of Barrett's Esophagus and Barrett's-Related Dysplasia: One Pathologist's Perspective**

presented by

**Dr. John R. Goldblum**, Chairman and Professor of Pathology, Cleveland Clinic Lerner College of Medicine. Case Western Reserve University . President of the Arthur Purdy Stout Society of Surgical Pathologists and Chair of the Education Committee for the United States and Canadian Academy of Pathology

### **Evening Guest Speaker**

**Role and Implementation of Informatics** presented by:

**Dr. Liron Pantanowitz**, UPMC Shadyside Hospital, Pittsburgh, PA., U.S.A.

## **Administration**

**Dr. Fiona Smaill**, Chair, Pathology & Molecular Medicine, McMaster University

**Dr. Mark Crowther**, Director, Hamilton Regional Laboratory Medicine Program (HRLMP), Hamilton Health Sciences

**Dr. Vena Alexopoulou**, Director, Anatomical Pathology

## **Program Directors**

**Dr. Monalisa Sur**, Anatomical Pathology

**Dr. Tariq Aziz**, General Pathology

**Dr. Andrew Don-Wauchope**, Medical Biochemistry

**Dr. Cheryl Main**, Medical Microbiology

**Dr. Stephen Hill**, Clinical Chemistry

**Dr. Jia-Chi (Jack) Wang**, Genetics

**Dr. Donald Arnold**, Transfusion Medicine Fellows

**Dr. John Fernandes**, Forensic Pathology

## **Judges**

***Dr. Liron Pantanowitz***

***Dr. John Goldblum***

***Dr. Mark Crowther***

***Dr. Fiona Smaill***

***Dr. Vena Alexopoulou***

# Program

## MDCL - 3020

9:00 am	Continental breakfast available in hallway, until 9:15 a.m. (Room 3020 is unavailable for access prior to 9:15)
9:15	Room opens.
9:30	Welcome by Dr. Fiona Smaill, Chair Department of Pathology and Molecular Medicine
9:35	Guest Speaker Introduction by Dr. Monalisa Sur, Program Director, Anatomical Pathology
9:40	George Frank Memorial Lecture <i>presented by</i> <b>Dr. John R. Goldblum</b> <b>"Controversies in the Diagnosis of Barrett's Esophagus and Barrett's-Related Dysplasia: One Pathologist's Perspective"</b>
10:45	10 min. break
10:55	Introduction to judges by Dr. Monalisa Sur, Anatomical Pathology Program Director Platform presentations begin. (15 mins per presentation - 10 to present; 5 for Q & A)
11:00	Maged Mansour, MB, PGY3
11:15	Ashwyn Rajagopalan, AP, PGY4
11:30	Sergey Pozdnyakov, AP, PGY2
11:45	Etienne Mahe, AP, PGY3
12:00	<u>LUNCH</u> in the hall. Posters on display in MDCL 3411 and 3412
1:15	Radenka Bozanovic, AP, PGY4
1:30	Kristin Hauff, CC, Fellow
1:45	Li Wang, MB, PGY3
2:00	Tarek Ezzat, AP, PGY2
2:15	Ali Amer, GP, PGY4
2:30	Miranda Schell, Anatomical Pathology, PGY2
2:45 - 4:00	Poster Judging. <b>Judges &amp; Authors to MDCL 3411 and 3412</b> Authors please stand by your poster. Listing of poster abstracts begins, pg. 15
Evening	Guest speaker at The University Club

# Program

MDCL - 3020

4:00 **To The University Club**

Cocktails, **University Club**, Upper Level, the Great Hall

5:15 *Awards Ceremony*, Upper Level, Great Hall. Presented by Dr. Smaill, Dept. Chair

5:30 Dinner

6:45 Residents' Research Day Evening Guest Speaker Introduction by  
Dr. Monalisa Sur, Upper Level, Great Hall

Evening Lecture **"Role and Implementation of Informatics"**  
presented by **Dr. Liron Pantanowitz**, UPMC Shadyside Hospital, Pittsburgh, PA., U.S.A.

# PRESENTATIONS

Con't...

## An Approach For Comparability Testing Of 20 Core Clinical Chemistry Analytes Measured Between Identical Roche P-Modular Platforms

**Mansour, M<sup>1</sup>**, Wang, L<sup>1</sup>, Clark, L<sup>2</sup>, and, Kavsak, P.<sup>1,2</sup>

<sup>1</sup>Department of Pathology and Molecular Medicine, McMaster University, <sup>2</sup>Juravinski Hospital Cancer Centre, Hamilton, ON

**Objective:** Comparability testing of the same analytes across laboratory platforms may be assessed in various ways (e.g., Clinical Laboratory Standards Institute/CLSI; C54-1 guideline, CVi—within subject biological variation). Our aim in the present study was to determine the difference in analyte concentrations between the same core chemistry analyzers at 1-laboratory site (i.e., lab-defined); and then prospectively evaluate these criteria at other hospital sites.

**Methods:** Over 22 days, 4 heparin plasma samples randomly selected for a pool (daily); was measured for 20 analytes on 2 Roche P-modular platforms within 1-laboratory. During this timeframe, external proficiency testing was acceptable for these analytes (2 surveys). The 3SD of the observed %difference in concentrations of the analytes between platforms was then calculated. Prospectively, over 5-months, 10 different pooled samples were then assessed at 3-laboratories/2 P-modulars each, for these analytes with the %difference assessed by the 3 criteria (lab-defined, CLSI, CVi).

**Results:** Of the 20 analytes, the lab-defined acceptable difference was higher than either CLSI or CVi criteria for urea (14% vs. 13%, 12%); AST (21% vs. 13%, 12%), ALT (27% vs. 17%, 24%), GGT (18% vs. 13%, 14%) and was lower for potassium (3% vs. 4%, 5%), total CO<sub>2</sub> (17% vs. 22%, N/A), and PO<sub>4</sub> (6% vs. 9%, 9%). Prospectively, for the 10 samples, only Mg (all 3-sites, 1 sample) and Glucose (1-site, 1 sample) resulted in %differences exceeding all 3 criteria. For Mg, the concentration was extremely low (average = 0.15 mmol/L), however, the discordant glucose repeat concentration was not (6.3 vs. 5.9 mmol/L).

**Conclusions:** The laboratory-defined criteria appear to have appropriately flagged discordant repeat results. Additional specimens (>4 for pool) may avoid extremely low concentrations, where imprecision of the assays may exceed the allowable %difference.



**In-Situ Follicular Lymphoma: a case series.****Rajagopalan A**<sup>1</sup>, Ross C<sup>2</sup>, Sur, M<sup>2</sup>.<sup>1</sup>Department of Pathology and Molecular Medicine, McMaster University; <sup>2</sup> Department of Pathology and Molecular Medicine, Juravinski Hospital

**Introduction:** Precursor lymphoid lesions have long been recognized in hematopathology. Monoclonal B-cell lymphocytosis has been established as a precursor to CLL, and NK-cell enteropathy was recently identified as a lymphoproliferative disease mimicking NK/T-cell lymphoma in the digestive tract. Neither of these lesions requires treatment in the absence of transformation to a more aggressive form. Similarly, the relationships between certain lymphomas and newly described associated atypical proliferations not meeting the WHO criteria for lymphoma have recently been investigated. In particular, the entities of in-situ follicular lymphoma and in-situ mantle cell lymphoma are being more frequently recognized in routine surgical practice. The former lesion is characterized by focal germinal center staining of a neoplastic follicle with BCL-2 in a background of a reactive lymph node, with otherwise preserved nodal architecture. As of yet, there is no established guidelines for treatment of these lesions, with most authors advocating a "watchful waiting" approach.

**Objectives:** To report five cases from this institution (from 2005-2011) of incidental in-situ follicular lymphoma. The morphologic, the immunohistochemical, and the clinical significance of this diagnosis will be discussed.

**Methods:** Four female patients (ages 55-68 years ) undergoing surgery with pelvic lymph node dissection (two for endometrial carcinoma, two for colonic adhesions for endometriosis) were noted to have the incidental finding of in-situ follicular lymphoma. One male patient (age 56 years) was diagnosed on an enlarged unilateral inguinal lymph node removed during surgery for ruptured femoral artery aneurysm.

**Results:** In the cases with pelvic lymph node dissection, one out of several reactive lymph nodes showed in-situ follicular lymphoma in an otherwise reactive lymph node with no architectural effacement. The neoplastic follicles showed expression of B cell and germinal center cell markers with BCL2 staining and a low Ki67 proliferation index. The reactive follicles, in contrast, were negative for BCL2 and showed a high Ki67 proliferation index. Similar findings were noted in the inguinal and mesenteric lymph nodes from the other three patients. Staging bone marrow in these five patients was negative. To date, none of the patients have demonstrated evidence of recurrence or progression to overt lymphoma.

**Conclusions:** In-situ follicular lymphoma is often an incidental finding and needs to be differentiated from "early" follicular lymphoma. Recognition of this entity is important, as no further treatment beyond surgical excision is yet recommended. However, long term follow up to better understand the natural history, the significance and the potential for malignant transformation in this group of diseases is needed.

**A patient with hypertrophic cardiomyopathy and acute transmural myocardial infarction**

**Pozdnyakov S**<sup>1</sup>, Fernandes J<sup>2</sup>,

<sup>1</sup>Department of Pathology and Molecular Medicine, McMaster University, Hamilton, ON; <sup>2</sup>Department of Pathology and Molecular Medicine, Hamilton General Hospital, Hamilton, ON

**Abstract:** Hypertrophic cardiomyopathy (HCM) is the most common cause of sudden cardiac death in the young. The understanding of the role of myocardial ischemia in pathophysiology of HCM has changed dramatically in the last few decades. It is now evident that microvascular dysfunction is very important component of this complex disease process, promoting left ventricular remodeling and impacting on clinical course and associated complications, such as sudden cardiac death (SCD) and myocardial infarction.

Our article presents one of the rare cases of extensive acute transmural myocardial infarction causing death in a young HCM patient. This case signifies a role of the ischemic intramural small vessel disease as a primary substrate of the SCD, arrhythmia, myocardial infarction and resultant myocardial scarring in HCM.

## Mathematical Modeling of Lymph Node Grossing

**Mahe ER**<sup>1</sup> (sole author)

<sup>1</sup> Department of Pathology & Molecular Medicine, McMaster University, Hamilton, Ontario

### Abstract:

**Background:** There are two schools of thought pertaining to lymph node grossing: that a lymph node be grossed with cuts made parallel to the long axis or that cuts be parallel to the short axis. The superiority of one approach over the other has not been rigorously proven. When grossing a lymph node, the three dimensional structure of the lymph node is reduced to a two-dimensional cut surface representation. If a metastatic focus is present, the detection of said focus should be improved if more cut surface area is available for histological examination.

**Methods:** By means of computer simulation, this study compared the detection of tumour foci (smaller than micrometastases) at randomly positioned foci in variously sized lymph nodes using the two techniques described above. In each case, the detection of the tumour was approximated by transection of the tumour focus.

**Results:** A thousand computer simulations with 1000 lymph nodes each were performed. In 98% of the lymph node sizes compared, the long axis grossing technique was optimal. The optimal and non-optimal techniques were then compared: tumour was detected in an average of 87.7 lymph nodes sectioned optimally and 86.7 lymph nodes sectioned non-optimally; this difference was noted to be significant by the Student's t-test.

**Conclusions:** Taken together, these results suggest that grossing with cuts made parallel to the long axis is adequate. This approach will be optimal 98% of the time with little improvement in detection rate in cases for which cuts made parallel to the short axis optimally maximize the cut surface area.

**Anaplastic Gangliogliomas – Case Series****Bozanovic R.**<sup>1</sup>, Lach B.<sup>1</sup><sup>1</sup> Department of Pathology & Molecular Medicine, McMaster University, Hamilton

**Introduction:** Gangliogliomas represent 1% of central nervous system neoplasms. Typically they occur in children with long history of intractable seizures and lesion in temporal lobe. Literature on anaplastic gangliogliomas with onset in late adulthood is limited to single reports and small case series. Here we present series of 39 cases.

**Methods:** We searched our institution's computerized database for gangliogliomas in period from 1985 to 2011. Clinical histories, radiological imaging, pathology reports and histological slides were reviewed. Histological grading was defined according to WHO criteria. Presence of glial and neuronal components was confirmed by immunohistochemical staining (GFAP, synaptophysin, chromogranin and neurofilament).

**Results:** 39 cases of gangliogliomas were identified, 17 in low and 22 in high grade category.

Grade N	Low grade GGL N=17	High grade GGL N=22
<b>Patient's age and clinical presentation</b>		
<b>Age</b> –yrs, average, (range)	26 (0.5 – 60)	59 (26 – 85)
<b>Childhood onset</b> - N, %	13 (76.5)	1 (4.5)
<b>Presenting symptom seizure</b> - N, %	13 (76.5)	10 (45.5)
<b>Interval from onset to histological diagnosis</b> –average, (range)	12 yrs (1 mo - > 45 yrs)	2.6 mo (3 days–24 mo)
<b>Tumor size</b> -cm	3.2 (0.5 – 9.0)	4.2 (1.6–9.3)
<b>Surgical resection</b>		
<b>Complete resection (CR)</b> - N, %	12 (70.6)	5 (22.7)
<b>Recurrence after CR</b> - N, %	1 (5.9)	3 (13.6)
<b>Follow-up and outcomes</b>		
<b>Follow-up data available</b> - N, %	16 (94.1)	18 (81.8)
<b>Expired</b> - N, %	1 (6.3)	13 (72.2)
F/U time –average, (range)	1 mo	17 (4-57) mo
<b>Alive</b> - N, %	15 (93.8)	5 (27.8)
F/U time –average, (range)	76 (5 – 285)mo	32 (2-102)mo

**Conclusion:** Gangliogliomas with onset in late adulthood have aggressive behaviour, in contrast to typical low grade lesions occurring in childhood. Their prognosis is still more favourable than in glioblastoma multiforme, with some lesions amenable for complete resection.

## Sweating the Small Stuff: A Quality Assurance Audit of Sweat Chloride Testing for Cystic Fibrosis Newborn Screening Follow-up

Hauff, K.<sup>1</sup>, Brick, L.<sup>2</sup>, Carroll, V.<sup>3</sup>, Grey, V.<sup>1,4</sup>, Pedder, L.<sup>3,4</sup><sup>1</sup>Department of Pathology and Molecular Medicine, McMaster University, <sup>2</sup>Department of Genetics, Hamilton Health Sciences, <sup>3</sup>Pediatric Cystic Fibrosis Clinic, McMaster Children's Hospital, <sup>4</sup>Department of Pediatrics at McMaster University, Hamilton, ON.

**Objectives:** Newborn screening (NBS) for cystic fibrosis (CF) was implemented in Ontario in 2008. Hamilton Health Sciences is one of five regional centers for NBS confirmatory testing. By assuring the sweat chloride test is performed correctly, we ensure consistent, reliable and timely follow-up for screen positive infants. Our aim was to investigate the quality of our confirmatory sweat chloride testing.

**Methodology:** We reviewed the data collected on all CFNBS positive infants identified by the NBS program from January 2010 to December 2010, inclusive. We examined the effects of gestational age, birth weight, ethnicity, CFTR mutations, and IRT values on both the sweat weight and results.

**Results:** In 2010, 66 patients were identified for confirmatory testing, the results are summarized below (**Table 1**). Sweat testing confirmed 9 CF affected infants (a 10<sup>th</sup> died prior to sweat testing). Of these, 5 initially revealed only 1 mutation by NBS. Our patients were a mean age of  $15 \pm 4$  days when first identified by the NBS program, and were seen for sweat testing within  $9 \pm 12$  days, (recommended standard: < 2 weeks). Our rate of insufficient sweat collection was slightly high, at 13%, (recommended standard: 5-10%).

**Conclusion:** Our results represent an estimated incidence of ~1:2000, somewhat higher than expected in a population of predominantly European descent. This is likely due increased identification of milder cases with the NBS. Our practices for confirmatory sweat testing of positive CFNBS infants are in line with the current recommendations. Minimal wait times for confirmatory testing allows earlier identification of CF patients (<3 months old) than prior to the implementation of CFNBS (mean age 3.6 years old). This is expected to result in overall improved health and outcomes due to a delay of bacterial colonization and better nutrition earlier in the course of disease.

CF NBS IRT + 2 CF Mutations	CF Status	N	Sweat Chloride Result (mmol/L)		Wait Time to First Sweat Test (days)	
			Median	Range	Mean	SD
	Affected	4	106	29-110	3	1
	Affected	5	33	17-76	3	3
	Carrier	48	17	0-49	10	13
	Carrier	2	18	15-20	6	5
	Unaffected	2	53	53	11	8

### Comparison between Abbott Precision Xceed Pro (PXP) and Nova Statstrip (STATSTRIP) Glucose Meters in Neonates

**Wang L**<sup>1</sup>, Sievenpiper J<sup>1</sup>, Thomaz M<sup>2</sup>, Balion C<sup>1,3</sup>, Fusch C<sup>2</sup> and Grey V.<sup>1,2,3</sup>

<sup>1</sup>Department of Pathology and Molecular Medicine, Faculty of Health Sciences, McMaster University; <sup>2</sup>Department of Pediatrics, Faculty of Health Sciences, McMaster University; and <sup>3</sup>Department of Laboratory Medicine, Hamilton Health Sciences, Hamilton, ON, Canada

**Abstract:** The lack of accuracy of point of care testing (POCT) glucose meters has limited their use in the diagnosis of neonatal hypoglycemia. Our previous study using the Abbott PCx suggested that hematocrit and low glucose concentrations in part contribute to the discordance. Abbott PXP and Nova StatStrip glucose meters are the two most recent models and the latter claims no hematocrit effect which is suitable for use in neonates.

**Objective:** To evaluate the performance of Abbott PXP and Nova StatStrip glucose meters; To assess the effects of hematocrit on glucose measurements by comparing the results of Abbott PXP and Nova StatStrip glucose meters with the glucose measurement on the laboratory analyzers.

**Methods:** All neonates who had a glucose test ordered at McMaster University Medical Centre and a hematocrit result within 24 hour were enrolled into the study. Blood samples were analyzed in the laboratory on the PXP, StatStrip and ABL 800 Flex Blood Gas analyzer (Radiometer). Hematocrit was measured on the Beckman-Coulter LH 750. Acceptable error was assessed at two recommended levels:  $\pm 15\%$  recommended for POCT and  $\pm 5\%$  recommended for diagnosis.

**Results:** The performance of the PXP and StatStrip is shown in the table. The difference in glucose concentration between the StatStrip and ABL ( $R=-0.0141$ ,  $p=0.8030$ ) was not dependent on hematocrit (22.8%-71.9%) but there was an inverse relationship with the PXP ( $R=-0.5174$ ,  $p<0.0001$ ).

Glucose (ABL)	Percent results within 5% ABL		Percent results within 15% ABL	
	PXP	StatStrip	PXP	StatStrip
1.4-15.8mmol/L(n=307)	31%	45%	78%	89%
$\leq 4$ mmol/L(n=152)	46%	43%	81%	82%
$> 4$ mmol/L(n=155)	49%	63%	75%	95%

**Conclusions:** Although the Nova StatStrip did not demonstrate dependence on hematocrit, this did not alter its performance. Neither Nova StatStrip nor Abbott PXP meets acceptable performance criteria for diagnosis of neonatal hypoglycemia.

**Cholesterol Granuloma of the Anterior Mediastinum Presenting as an Incidental Intraoperative Anterior Mediastinal Mass**

**Ezzat, T.**<sup>1</sup>, Alowami, S.<sup>2</sup>

1. Anatomic pathology resident, McMaster University, Hamilton ON; 2. Anatomic pathology staff physician, St. Joseph's Hospital, Hamilton ON

**Introduction:** Cholesterol granulomas are frequently found in the temporal bone secondary to inflammatory ear disease. They have been rarely reported in other regions such as the brain, orbit, kidney, breast, and anterior mediastinum, the latter of which were associated with prior trauma and multilocular thymic cyst. There has been a case of multiple cholesterol granulomas associated with MEN-1 syndrome.

The pathogenesis involves a traumatic or inflammatory event inciting hemorrhage. Subsequent erythrocyte degeneration causes cholesterol crystalline complexes to form and provoke a foreign-body reaction. This process can result in a slow-growing mass which can be locally aggressive. Hyperlipidemia and impaired lymphatic drainage may also play a role in pathogenesis. Osseus metaplasia is a rare finding in cholesterol granulomas.

**Case report:** A 75 year-old male with a history of heart and vascular disease, smoking, COPD, dyslipidemia, and prior work-related crush injury had undergone urgent cardiac surgery for acute myocardial infarction. Pre-operative chest radiograph showed a questionable density in the anterior mediastinum that was attributed to the first rib. During surgery, a pair of firm, well-circumscribed masses was found in the anterior mediastinum and was excised. The patient recovered uneventfully.

The dimensions of each nodule were 3.0 x 3.0 x 2.0 cm. Cut surfaces were granular. One nodule was diffusely hemorrhagic and focally calcified, while the other was yellow and fatty.

The specimen was extensively sampled. Microscopic examination showed large needle-shaped crystals surrounded by multinucleate giant cells and hemosiderin-laden macrophages consistent with cholesterol granuloma, with foci of osseus metaplasia.

**Conclusion:** Our report describes a cholesterol granuloma of the anterior mediastinum with osseus metaplasia. This is the first time this rare entity has been found with osseus metaplasia in this location. In our case, it was likely due to prior trauma.

## Critical Diagnoses In Anatomical Pathology in Ontario

**Amer A.<sup>1</sup>**, Chorneyko K.<sup>1</sup>

<sup>1</sup>Department of Pathology and Molecular Medicine, McMaster University, Hamilton, ON

### Introduction:

In clinical pathology, “critical values” are results with life-threatening consequences that require immediate treatment and guidelines are in place for contacting clinicians and documenting this contact. In Anatomical Pathology, cases that require immediate treatment or prompt evaluation are referred to as critical diagnoses (CD). Although there are American guidelines for CDs, there are no Canadian guidelines at the provincial or national level.

### Purpose of the study:

This survey will help to better define the concept of CDs in Ontario. The data collected will give insights into the pattern of practice in Ontario and may inform future guideline development or suggest recommendations for CDs policies.

### Method:

A list of CDs was created based on studies showing consensus about most common CDs in Anatomical Pathology. A voluntary survey was designed using “Survey Monkey™”, to discover what is considered a CD as well as how it is communicated and documented. It was sent to a random cohort of 85 pathologists representing a spectrum of pathology practices across Ontario. All contact information was collected from public registries and directories.

### Results:

The response rate was 30.5 %. Eighty eight percent were in agreement with the CDs listed. Differences of opinion were present regarding the appropriate notification process. Eighty four percent of respondents do not have a policy for CDs in their institutes. Only one respondent believed that CDs should be based on the professional judgment of the pathologist regardless of the diagnosis.

### Conclusions:

Pathologists in general agree about the types of cases which constitute CDs; however there are differences about the most appropriate notification process. The majority of departments do not have CDs policies in place. Patient safety may be enhanced by guidelines about CDs and the manner in which they should be relayed. Further data collection across the country would be beneficial to develop recommendations about CDs in Anatomical Pathology in Canada.

**Comedonecrosis in Two Cases of Poorly Differentiated Adenocarcinoma of the Ampulla of Vater****Schell M<sup>1</sup>**, Radhi J<sup>2</sup><sup>1</sup> Department of Pathology and Molecular Medicine, McMaster University<sup>2</sup> Department of Pathology and Molecular Medicine, McMaster University Medical Centre

**Background:** Adenocarcinomas of the ampulla of Vater are rare with an estimated incidence of less than 1/100 000. In general, this disease is thought to have a better prognosis than pancreatic cancer (5 year survival rate of 45%) because it is generally detected at an early stage, due to the location of these tumors. They can have intestinal or biliary features. The most established prognostic factor to date is lymph node involvement. Histological differentiation amongst others has also shown importance in outcome. In other disease sites, comedonecrosis is an unfavorable marker for prognosis and represents a biologically aggressive variant.

**Objectives:** To report two cases of poorly differentiated ampullary carcinoma with the uncommon histological feature of comedonecrosis; their morphologic features and immunohistochemical profile are highlighted.

**Methods:** The two cases were identified at the Pathology Department McMaster University Medical Center. The H & E and immunohistochemistry slides were reviewed. A search of the electronic database of Hamilton Health Science pathology reports revealed no similar cases. The slides from the other reported poorly differentiated ampullary carcinomas were reviewed and none of which displayed comedonecrosis. A web-based literature search did not return any previous description of this histological feature.

**Results:** Both cases identified showed extensive lymph nodal metastasis. The tumor morphology was poorly differentiated adenocarcinoma with areas of comedo-like necrosis. Immunohistochemistry markers were focally positive for CK7, CK20, and CEA with variable positivity for CK19 and p53. All neuroendocrine markers were negative.

**Conclusions:** These two cases demonstrate a histologic variant of poorly differentiated adenocarcinoma of the ampulla of Vater with extensive regional nodal involvement. As lymph node metastasis heralds a poorer prognosis in ampullary cancers, this described pattern of comedonecrosis may represent a feature of ampullary adenocarcinoma with a worse-than-typical prognosis.

# POSTERS

Judging will commence in MDCL - 3411 and 3412 at 2:30 p.m.

To qualify for awards, authors must be with their poster during this time to answer questions.

## Judges

*Dr. Liron Pantanowitz*

*Dr. John Goldblum*

*Dr. Mark Crowther*

*Dr. Fiona Smaill*

*Dr. Vina Alexopoulou*

## **Posters on display:**

**Troy Grennan**, Medical Microbiology, Fellow

**Salaheddin Abouanaser**, Medical Microbiology, PGY4

**Lori Edwards**, Anatomical Pathology, PGY4

**Etienne Mahe**, Anatomical Pathology, PGY3

**Emad Abdulrahman**, General Pathology, PGY3

**Hetal Talati**, General Pathology, PGY4

**Jocelyn Srigley**, Medical Microbiology, PGY5

**Kika Veljkovic**, Clinical Chemistry, Fellow

**Leena Narsinghani**, General Pathology, PGY3

**Pooja Vasudev**, Anatomical Pathology, PGY5

**Prevalence of *Streptococcus pneumoniae* colonization in nursing home elderly: comparison of conventional culture and polymerase chain reaction**

**Grennan T**<sup>1,2</sup>, Leto D<sup>1,2</sup>, Luinstra K<sup>3</sup>, Petrich A<sup>4</sup>, Smieja M<sup>2,5,6</sup>, Loeb M<sup>2,5,6</sup>, and Johnstone J<sup>1,5</sup>

<sup>1</sup>Department of Medicine, Division of Infectious Diseases, McMaster University, Hamilton, ON; <sup>2</sup>Department of Pathology and Molecular Medicine, McMaster University, Hamilton, ON; <sup>3</sup>St. Joseph's Hospital, Hamilton, ON; <sup>4</sup>Department of Laboratory Medicine, The Hospital for Sick Children, Toronto, ON; <sup>5</sup>Michael G. DeGroote Institute for Infectious Disease Research, McMaster University, Hamilton, ON; <sup>6</sup>Department of Clinical Epidemiology and Biostatistics, McMaster University, Hamilton, ON, Canada

**Background:** Though the burden of disease due to *Streptococcus pneumoniae* is high in the elderly, the proportion of nursing home (NH) elderly colonized with *S. pneumoniae* outside of outbreak settings has not been well described. Recent advances in molecular testing may mean that polymerase chain reaction (PCR) performs better than conventional culture of *S. pneumoniae*. In this study we sought to describe the proportion of elderly colonized with *S. pneumoniae* in a non-outbreak setting using both conventional culture and PCR.

**Methods:** In December 2009, nasopharyngeal (NP) swabs (Copan ESwabs) were collected from 123 asymptomatic NH residents and plated on 5% sheep blood agar within three hours of collection. Following 24 hours of incubation at 35°C, 5% CO<sub>2</sub>, *S. pneumoniae* was identified using colonial morphology, alpha-hemolysis and optochin disk susceptibility. A sensitive and specific real-time PCR was also performed on the NP samples using methods adapted from McAvin *et al* (J Clin Microbiol 2001 ;39:3446-51).

**Results:** The mean age was 86 years, 71% were female and all had at least one co-morbidity. 78/123 (63%) had received pneumococcal vaccination within the last 5 years, and only 34/123 (28%) had exposure to children. Using conventional microbiological culture, the yield for recovery of *S. pneumoniae* from NP swabs was 0/123 (0%, 95% CI: 0-3.6%) for the aerobic conditions. Real-time PCR yielded 7/123 (5.7%; 95% CI: 2.6-11.5%) positive samples for *S. pneumoniae* (p=0.02). There were no differences in characteristics between colonized and non-colonized participants.

**Conclusions:** Despite the high incidence of infection due to *S. pneumoniae* in the NH elderly, the proportion colonized with *S. pneumoniae* outside of the outbreak setting is very low raising the possibility that the elderly may be less able to control colonization than younger individuals. PCR was more sensitive than culture and will be a useful tool for future colonization studies.

**Evaluation of the VITEK 2 system for rapid direct identification and susceptibility testing of gram-negative bacilli from positive blood cultures.**

**Abouanaser S<sup>2</sup>**, Nuri K<sup>2</sup>, Dourmound P<sup>1</sup>, Bondy K<sup>1</sup>, Monkman L<sup>1</sup>, Dale S<sup>1</sup>, And, Main C<sup>1 2</sup>

<sup>1</sup>Hamilton Regional Laboratory Medicine Program, <sup>2</sup>McMaster University, Hamilton ON

**Objective:** Rapid identification and susceptibility testing for GNB (gram negative bacilli) has the potential to improve patient therapy, outcome and improve workflow in the laboratory. To assess this, we evaluated direct identification of GNB using VITEK 2 (Biomerieux) and by matrix-assisted laser desorption/ionization time of flight (MALDI-TOF) mass spectrometry.

**Methods:** Blood cultures with GNB identified in the BacT/Alert culture system (Biomerieux) were inoculated to the VITEK 2 ID-GN card and AST-GN24 card following differential centrifugation. Identifications and susceptibilities were compared to standard identification methods.

**Results:** One hundred fifteen positive aerobic blood cultures were evaluated using VITEK 2. Eighty four isolates (73%) were reported to a confidence level of  $\geq 90$ , 18 isolates (15.7%) were reported to a confidence level of  $< 90$  and 13 isolates (11.3%) were unidentified. Correct identification to the species level was achieved in 94% (79/84) when the confidence level was  $\geq 90$ . Five misidentified organisms were *A. calcoaceticus*, *E. coli*, *K. pneumoniae* and 2 *K. oxytoca* when confidence level  $>90$  % was used. The susceptibilities of 79 strains had complete MIC agreement for 98.8% of the drugs tested. Of the disagreements, 1 had a very major error when a *Citrobacter* which was resistant to piperacillin-tazobactam was interpreted as susceptible, 3 had major errors and 9 were minor errors. Hands on technologist time was less than one hour.

A subgroup of 45 isolates were evaluated by MALDI-TOF mass spectrometry. We were able to confirm the identification of 95.5% of these isolates directly from blood cultures.

**Conclusions:** This method shortens TAT, and has the potential to improve patient care with minimal increased cost. By using the criteria of a 90% confidence level with the VITEK 2 identification platform, 69% of gram negatives were correctly identified and the very major error rate for susceptibility testing was low. The MALDI-TOF shows greater potential for direct identification of gram negative bacilli in blood cultures. Further work is needed to fully evaluate these methods.

**Title:** Characterization of B-cell Lymphoma Unclassifiable with Features Intermediate between Diffuse Large B-cell Lymphoma and Burkitt's Lymphoma: A Ten Year Review.

**Edwards. L.** Bhagirath, V, Krakow, E, Keng, C, Lytwyn, A, Ross, C, Thebane, L, Cheng, E and Sur, ML. McMaster University, Hamilton, Ontario, Canada.

**Background:** Little is known about the behavior of "B-cell lymphoma unclassifiable (BCLU) with features intermediate between Diffuse Large B-cell lymphoma (DLBL) and Burkitt Lymphoma (BL)".

**Design:** This is a ten-year retrospective examination of the clinical characteristics, survival, treatment response and molecular profile of BCLU (n=34) compared to DLBL (n=97). Two pathologists together reviewed 141 cases using 2008 WHO criteria for BL, BCLU and DLBL. BCLU cases with sufficient material were tested for Bcl2 and MYC genetic abnormalities.

**Results:** BLCU had more frequent CNS involvement ( $p=0.01$ ), and bulky disease ( $p=0.02$ ) than DLBL. There was no significant difference in age, gender, International Prognostic Index, Ann Arbor stage, or bone marrow involvement. Median overall survival (OS) and progression-free survival (PFS) for BCLU was 330 and 221 days respectively, compared to 837 and 664 days for DLBL ( $p<0.02$ ). Hazard Ratio (HR) was 2.5 (95%CI 1.2-5.2,  $p=0.048$ ) for OS and 2.0 (95%CI 1.0-3.9,  $p=0.048$ ) for PFS. Four BCLU patients (12%) received BL chemotherapy regimes, while 24 (71%) received CHOP-based therapy. Disease progression while on treatment occurred in 9 (33%) of BCLU and 8 (10%) of DLBL ( $p=0.03$ ). Nine of 24 (36%) BCLU tested had concurrent Bcl2 and MYC genetic abnormalities, called double hits (DH). OS for BCLU with DH was worse than non-DH, HR 13.8; (95%CI 2.3-83.6,  $p=0.004$ ).

**Conclusion:** Compared to DLBL, BCLU patients present with more advanced disease, progress while on treatment and have a poorer survival. BCLU with DH may have a worse prognosis, but these findings are limited by the small sample size. This is the first study to demonstrate that the clinical outcome of the new BCLU entity appears to be distinct from DLBL and further studies into more effective treatment regimes are necessary.

**Micropapillary Carcinoma of the Breast****Mahe E**<sup>1</sup>, Farag M<sup>2</sup>, Boutross-Tadross O<sup>1</sup><sup>1</sup> Department of Pathology & Molecular Medicine, McMaster University, Hamilton, Ontario; <sup>2</sup> CSAT program, Memorial University, St. John's, Newfoundland**Abstract:**

Micropapillary carcinoma of the breast is a rare entity defined histologically by the presence of clusters of tumor cells present within clear spaces and can occur as a pure form or mixed with other histologic types. The literature suggests that it is aggressive in comparison to Invasive Carcinoma NOS.

**Objectives:** We reviewed all breast excisions from MUMC from 2002 to 2009 for the presence of micropapillary features. We subsequently compared the pathologic features of those cases with predominantly micropapillary histomorphology (>90% of invasive tissue showing features of micropapillary morphology, PM), those with composite features (having between 1% and 90% micropapillary features, CM) and those without a micropapillary component (NM).

**Methods:** A list of breast cancer cases was obtained from Meditech and refined to include only excision specimens for invasive disease for which slides were available. Each case was classified as PM, CM or NM. The complete pathology reports were reviewed for age, laterality, size, Grade, lymphovascular invasion, skin/nipple involvement, lymph node metastases, stage (as defined in the AJCC 7th Edition), ER, PR and Her2 receptor status (based on current College of American Pathologists Guidelines).

**Results:** Of 326 invasive breast cancers, 47 showed a variable micropapillary component; and only 14 cases were PM. The only statistically significant differences between PM/CM and NM were greater likelihood of lymphovascular invasion and ER positivity in the former ( $p = 0.0034$  and  $0.038$ , respectively). The only statistically significant difference between PM and CM was greater likelihood of Her2 positivity in the former ( $p = 0.037$ ; this difference may have been influenced by the low number for which Her2 was available).

**Discussion:** Our data suggest few pathologic differences between PM, CM and NM. We hope that this group of cases may lend itself to future studies exploring the potential differences between micropapillary and non-micropapillary breast cancers.

**Papilocystic Variant of Acinar Cell Pancreatic Carcinoma****Emad Abdulrahman, Jasim Radhi****Abdulrahman E<sup>1</sup>**, Radhi J<sup>1</sup><sup>1</sup> Department of Pathology & Molecular Medicine, McMaster University, Hamilton, Ontario**Abstract**

Acinar cell carcinoma of the pancreas is a rare tumor and account for less than 2% of all pancreatic carcinoma. These tumors are commonly large well-circumscribed solid and highly cellular lesions. Recent literature review showed occasional rare cases with papillary or papilocystic growth pattern that can be mistaken for mass forming cystic neoplasms of the pancreas. Cystic pancreatic tumors represent a diverse collection of tumors with varied malignant potential and clinical presentation. The differential diagnosis includes intraductal papillary mucinous neoplasms (IPMNS), cystic neuroendocrine tumors and in female mucinous cystic neoplasms. However, these tumors carry more indolent and protracted clinical course than acinar cell carcinoma. The correlation of clinical, radiographic, histologic and immunohistochemical findings would be helpful to establish the accurate diagnosis and management. We report a large 10 cm pancreatic tumor with papilocystic pathology features involving the pancreatic head. By immunohistochemistry, the tumor cells were positive for CAM 5.2, amylase, trypsin and focally for synaptophysin, and negative for vimentin, insulin, glucagen, and somastostatin Electron microscopy confirmed the presence of zymogen granules characteristic of acinar cell carcinoma

**Apocrine adenocarcinoma of the vulva: A Rare Case Report**

**Talati H<sup>1</sup>**, Daya D<sup>1</sup>, and, Alowami S<sup>1</sup>

<sup>1</sup>Department of Pathology and Molecular Medicine, Juravinski Hospital and Cancer Centre

**Introduction:** Cutaneous vulvar carcinomas are predominantly of squamous cell carcinoma type. Primary vulvar adenocarcinomas are rare tumors with poorly understood histogenesis. They are classified into extramammary Paget's disease, sweat gland carcinomas, and "breast-like" adenocarcinomas of the vulva. Adenocarcinomas, originating from Bartholin glands, can also present as vulvar adenocarcinoma. Rare adenocarcinomas with apocrine features have been described in the literature. Origin of these neoplasms from the native apocrine sweat glands or from anogenital mammary-like glands is still debatable.

**Case report:** A 67 years old female presented with an enlarging vulvar lesion which appeared cystic clinically. Her past medical history included the remote history of treated lymphoma, the details of which was not available. There was no history of apocrine or adenexal tumor elsewhere in the body. Clinically there was no regional lymph node enlargement.

Excision biopsy of the left labial tumor was received in the histology department. The surgical specimen contained pink, tan hair bearing fragment of skin measuring 2.7 x 2.0 x 1.8 cm. The resection margin was inked. Serial sectioning of the specimen revealed nodular dermal lesion.

Microscopic examination revealed fairly well circumscribed but unencapsulated dermal nodule with features of adenocarcinoma. The cells showed apocrine histological features with increased mitosis and focal necrosis. Focal involvement of the deep inked resection margin was identified. The overlying epidermis was unremarkable. The carcinoma cells expressed positive staining for GCDPF-15, CEA, CK7 and EMA confirming the apocrine nature of the tumor. The cells were negative for ER/PR, CK20, LCA, CK5/6, HepPar 1 and WT-1.

**Conclusion:** Our report describes a rare case of primary apocrine adenocarcinoma of the vulva. While we acknowledge the controversial histogenesis, the absence of normal mammary-like glands in the vicinity of the tumor and negative immunostaining for ER and PR are supportive of the native sweat gland origin.

## Identification of Yeast from Blood and Sterile Fluid by Matrix-Assisted Laser Desorption/Ionization-Time of Flight Mass Spectrometry

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### Abstract:

**Objectives:** MALDI is a rapid method for identification of organisms based on analysis of large organic molecules. This study assessed the accuracy of MALDI (Bruker Daltonics, Germany) in the identification of yeast from blood and sterile fluid cultures.

**Methods:** Four protocols were tested on 18 well-characterized isolates using direct smears and extracted isolates from multiple media to optimize the identification scores. Consecutive blood and sterile fluid isolates from March-October 2010, and 8 additional isolates (n = 60), were then retrospectively identified using MALDI. Frozen isolates were subcultured twice to Sabouraud agar and incubated for 48 hours. MALDI was performed on direct and extracted smears using Compass 1.2 SRI for FLEX series. Results were compared to conventional identification (microscopy, urea, Vitek2 YST, API20CAUX).

**Results:** The clinical isolates tested were 12 different *Candida* species (n = 56), *Trichosporon inkin* and *T. mucoides* (n = 2), and *Cryptococcus neoformans* (n = 2). Based on results from the optimization phase, a score greater than 1.900 was found to be accurate for identification to the species level, which is lower than the manufacturer's recommendation of 2.300 to 3.000. The majority of isolates (45/60) could not be identified by performing MALDI on a direct smear. Extracted isolates were correctly speciated in 96.7% (58/60). The 2 isolates (*C. famata*, *C. saitoana*) that were incorrectly identified were not in the MALDI database. The test procedure took 1-2 minutes on direct smears and 20-30 minutes on extracted isolates.

**Conclusions:** MALDI of extracted isolates is a rapid and accurate method for identification of clinically significant yeasts.

**Comparison of Monomeric Prolactin Levels Following Macroprolactin Precipitation by PEG6000 And PEG8000**

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**Background:** Prolactin is a commonly measured analyte in investigations of infertility and hypothalamic-pituitary disorders. The circulating prolactin consists of active monomeric prolactin and higher molecular weight (MW) forms, including inactive macroprolactin. Macroprolactin interferes with prolactin immunoassays, contributing to increased prolactin levels, and potential misdiagnosis of hyperprolactinemia. Prolactin measurement pre- and post-polyethylene glycol (PEG) precipitation of macroprolactin is an accepted screening method for macroprolactin in hyperprolactinemic samples. Post-PEG monomeric prolactin reference intervals have been established for current prolactin immunoassays using PEG with MW of 6000 (PEG6000) (*Clin Chem* 2008;54:1673-1678). However, our lab and others (*Clin Chem* 2006;52:1366-1372) have used PEG with MW of 8000 (PEG8000) for macroprolactin precipitation.

**Objective:** To confirm the published monomeric prolactin reference interval we compared the post-PEG prolactin levels between PEG6000 and PEG8000.

**Methods:** Specimens referred for macroprolactin screen between October 2010 and February 2011 (n = 29) were split, and subjected to simultaneous PEG6000 and PEG8000 precipitation. Pre- and post-PEG prolactin levels were measured by Roche Elecsys immunoassay (coefficient of variation [CV]: 2.9% at 8mg/L, and 3.2% at 47mg/L). Post-PEG8000 prolactin levels were compared to post-PEG6000 prolactin levels by Passing-Bablok regression analysis and Altman-Bland difference plot using Analyse It software v2.22.

**Results:** The CV for precipitation was 6.1% at 39mg/L for PEG6000, and 9.3% at 37mg/L for PEG8000. Passing Bablok regression showed the fit of  $-1.02 + 0.95x$ . This demonstrated a significant constant bias (95% confidence interval [CI]: -2.00 to -0.11), and a non-significant proportional bias (95%CI: 0.93 to 1.00). The Altman-Bland analysis showed a bias of -8.8% (95%CI: -11.1% to -6.6%).

**Conclusion:** There is no clinically significant difference between post-PEG6000 and post-PEG8000 prolactin levels. However, a significant constant bias suggests laboratories that use PEG8000 should exert caution when reporting monomeric prolactin using post-PEG reference intervals established with PEG6000.

**Project Title: High Fat Diet results in Significant Changes in Visceral Adipose Tissue in a Rat Model of Diet induced Obesity****Authors:** Narsinghani L<sup>1</sup>, Don-Wauchope AC<sup>1</sup>, Holloway AC<sup>2</sup>, El-Zimaity H<sup>3</sup>.<sup>1</sup>Department of Pathology and Molecular Medicine and Medicine; <sup>2</sup>Dept of Obstetrics and Gynecology, McMaster University, Hamilton; <sup>3</sup>Dept of Laboratory Medicine and Pathobiology, University of Toronto, Toronto.**Abstract****Introduction:** Globally obesity has reached epidemic levels. Research evidence shows that obesity is associated with a state of chronic systemic inflammation with adipose tissue as the major site of damage. An increase in adipose tissue macrophages (ATMs) and typical "crowns" of macrophages have been described in obesity. However, much less is known about the extent and relevance of muscle tissue macrophages in obesity.**Objective:** With this project we sought to compare the macrophage counts in different compartments of adipose and muscle tissue in an animal model of diet induced obesity. We also wanted to study changes in the cell size of adipocytes in obesity.**Methods:** Sibling pairs (male and females) from 3 litters were randomized to receive either control or high-fat diet from weaning. At 39 weeks of age, fat (visceral and subcutaneous) and muscle (skeletal and cardiac) were collected for histological review and assessment of macrophage count using immunohistochemical stain ED1 (rat homologue of CD68 macrophage marker).**Results:** The macrophage count was significantly increased in the visceral fat of animals fed the high fat diet (p value = 0.0043). The macrophage count in subcutaneous fat, skeletal muscle and cardiac muscle did not show any significant association with diet. Adipocyte cell size was significantly increased both in the visceral and subcutaneous fat of animals fed the high fat diet (p = 0.0016 and p = 0.0066 respectively). There is a correlation between ATMs and adipocyte size in visceral fat but not in subcutaneous fat.**Conclusion:** These findings support a hypothesis that visceral adipose tissue inflammation rather than systemic inflammation is the source of chronic inflammation in obesity.

**Chromosome 17 polysomy and monosomy as biomarkers in women with locally advanced breast cancer (LABC).**

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**Background:** LABC patients rarely achieve complete pathological response (pCR). HER-2/*neu*, ER/PR, Ki-67 and p53 have been studied as biomarkers. However, results have been conflicting. Chromosome 17 (Ch17) harbours oncogenic genes such as HER-2/*neu*, p53, among others. The behaviour of tumours with aberration in the copy number of this chromosome (either polysomy or monosomy) is unclear, but these tumours may identify patients that respond differently to current treatment.

**Objectives:**

1. To determine if Ch17 polysomy/monosomy as detected by fluorescent *in situ* hybridization (FISH) on the pre-treatment needle core biopsy (NCB) of the breast, associated with a lower rate of pCR in LABC patients?
2. To determine if there is an association between the rate of pCR and tissue expression of Ki-67, p53 and ER/PR/HER-2?

**Methods:** Patients were identified from the Pathology Departments of HRLMP, and from JCC database (2007- 2010). Immunohistochemistry was performed on the NCB specimens to test for ER, PR, p53 and Ki-67 expression. HER-2/*neu* status, Ch17 polysomy (Ch17 probe (CEP17) signal/nucleus  $\geq 3$ ) and monosomy (CEP17 signal/nucleus  $< 2$ ) were determined from FISH results. Two pathologists, who were blinded from the core biopsy results, reviewed each mastectomy case slides to assess for pCR. Chi-square ( $\chi^2$ ) test was performed, and a p-value  $< 0.05$  was considered statistically significant.

**Results:** Normal Ch17 expression, polysomy, and monosomy was identified in 46, 14, and 5 patients, respectively (N=65). Of those with normal Ch17 expression there were 6 (14%) pCR and 4 (26%) pCR among polysomic tumours ( $p = 0.172$ ). None of the monosomic tumours achieved pCR. Higher proportion of ER-/PR- and HER-2+ tumours achieved pCR ( $p = 0.007, 0.001$ , respectively). The results of p53 and Ki-67 are pending.

**Conclusion:** Monosomic tumours demonstrated higher resistance to chemotherapy, suggesting that they need to be treated differently. However, the small sample size prevents us from deriving definite conclusions. The role of polysomy as a biomarker remains unclear. Our data strongly suggests that ER-/PR- and HER-2+ tumours achieve a higher rate of pCR.



## THANK YOU

For sharing in our Residents' Research Day, 2011

We hope to see you again, next year