New Horizons in Cancer Research: Delivering Cures Through Cancer Science

November 6-9, 2017 • Shanghai Marriott Hotel Parkview • Shanghai, P.R. China

Poster Session A – Tuesday, November 7, 2017, 1:00-3:30 p.m.

Tumor Biology*

A03 Identification of prognostic biomarkers by combined data mining analysis and crispr-cas9 gene knockout system in pancreatic cancer. <u>Bin Liu</u>, Department of Surgery, Universitätsklinikum Erlangen, Erlangen, Germany.

A04 A high-throughput 3D tumor spheroid screening method for drug discovery using imaging cytometry. <u>Ting Zhang</u>, Nexcelom Bioscience, Shanghai, PR China.

A05 Inhibition of AKT and SRC reactivate the tumor suppressor functions of DLC1 by distinct mechanisms. Brajendra Tripathi, National Cancer Institute, National Institutes of Health, Bethesda MD, Maryland, United States.

A06 KMT2D promotes esophageal squamous cell cancer lymph node metastasis by interacting with **NF-κB** and facilitating STC1 transcription. <u>Tao Chen</u>, Zhongshang Hospital of Fudan University, Shanghai, PR China.

A07 Differential Regulation of Apoptosis and Senescence by the miR-449 Family microRNAs and Its Implications in Tumor Micro-environments of NSCLC. Chun-Yu Cho, National Institute of Cancer Research, National Health Research Institutes, Miaoli, Taiwan.

A08 SIK2 serves as a modulator for Wnt pathway to regulate cancer cell stemness. Zhuoxian Rong, Central South University, Hunan, PR China.

A09 Endothelial specific Notch signal promotes tumor vessel normalization via facilitating EndMT. Xianchun Yan, FMMU, Xi'an, PR China.

A11 Glutamine synthetase promotes irradiation resistance via facilitating nucleotide metabolism and subsequent DNA repair. Shujun Fu, Xiangya Hospital, Central South University, Hunan, PR China.

A12 CTAB reversed drug-resistance mediated by AMPK-HIF- 1α -P-gp pathway in breast cancer. <u>Yue Pan</u>, Dalian University of Technology, Liaoning, PR China.

A13 Human mesenchymal stem cells promote ovarian cancer progression: the role of plateletactivating factor. <u>Tong Gao</u>, Obstetrics and Gynecology Hospital of Fudan University, Shanghai, PR China.

A14 Phenotypic Transition Contributes to Small Cell Lung Carcinoma Metastasis through TAZ Downregulation. Yujuan Jin, Institute of Biochemistry and Cell Biology, Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences, Shanghai, PR China.

A15 In vivo CRISPR screening unveils UTX as an important epigenetic regulator in lung tumorigenesis. Qibiao Wu, Institute of Biochemistry and Cell Biology, Shanghai Institute for Biological Sciences, Shanghai, PR China.

A16 Berberine reversed Hypoxia-induced Chemoresistance by regulating AMPK HIF-1 α in Breast Cancer. Min Cao, Dalian University of Technology, Liaoning, PR China.

A17 The secretion mechanism of the increased circulating galectin-3 in the metastasis of breast cancer. Lei Wang, Shandong university, Shandong, PR China.

A21 MicroRNA-486-5p suppresses NSCLC via directly targeting RPS6KA1. <u>Lei Ding</u>, School of Life of Sciences, Shanghai University, Shanghai, PR China.

A22 Tissue-specific feature of whole genome sequencing aids tissue-mapping in plasma. <u>Han Liang</u>, Beijing Genomics Institute - Shenzhen, Guangdong, PR China.

A24 Overexpression of OLA1 may be associated with gemcitabine resistance of pancreatic cancer.<u>Jianzhou Liu</u>, Dalian University of Technology, Liaoning, PR China.

A25 Arrestment of tumorigenesis by HNRNPC repression via dsRNA-induced IFN response in breast cancer cells. Yusheng Wu, Tsinghua University, Beijing, PR China.

A26 The impact of Mll3 restoration on tumor maintenance. Mei Chen, State Key Laboratory of Biotherapy, West China hospital, Sichuan University and Collaborative Innovation Center., Sichuan, PR China.

A27 Tumor-infiltrate immunosuppression seems predictive of efficacy of the checkpoint inhibitors in a population-based trial syngeneic tumors. Annie An, Crown Bioscience, Santa Clara, United States.

A28 The importance of cellular oxygenation measurements in the analysis of hypoxia-induced signalling and related metabolic adaptation. Ian Hayes, Bio-Gene Technology Ltd, Shatin, Hong Kong.

A29 CD163+ Macrophages Stabilize ERα protein through A20-mediated Ubiquitination Modification to Sensitize Endometrial Cancer Cells to Estrogen. Qiaoying Lv, Obstetrics and Gynecology Hospital, Fudan University, Shanghai, PR China.

A30 clonal evolution of Intrahepatic Cholangiocarcinoma. <u>Liangqing Dong</u>, Zhongshan Hospital, Shanghai, Shanghai, PR China.

A34 Functional Mechanism of CTDP1 regulating the activity of FA pathway in Breast Cancer. Wenfeng Hu, Xiangya Hospital, Central South University, Hunan, PR China.

*Please see abstracts A80-A83 below for additional abstracts in this category

Clinical Research

A36 Clinical response of the novel activating ALK-I1171T mutation in neuroblastoma to the ALK inhibitor ceritinib. Jikui Guan, Gothenburg University, Gothenburg Sweden, Sweden.

A41 Long-term outcomes of endoscopic submucosal dissection for early cancer and high grade dysplasia in colorectum. Tao Chen, Zhongshang Hospital of Fudan University, Shanghai, PR China.

A43 Repurposing itraconazole for an anti-cancer agent: interim analysis of a window of opportunity study. Roze Nakata, Hyogo College of Medicine, Nishinomiya, Japan.

A44 Individual Diagnosis of Adult Diffuse Gliomas into the EM/PM Molecular Subtypes. <u>Jiuyi Li</u>, Beijing Key Labratory of Gene Resource and Molecular Development, Labratory of Neuroscience and Brain Development, Beijing Normal University, Beijing, PR China.

A47 Detection of emerging mutation in metastatic liver tumor by liquid biopsy in patients with colorectal cancer. <u>Hiroyasu Furuki</u>, Nippon Medical School Hospital, Tokyo, Japan.

Clinical Trials

A49 A phase I study to evaluate the safety of multi-antigen stimulated tumor specific cellular therapy (MASCT-I) in patients with advanced solid tumors. Xiaoshuang Li, Sun Yat-sen University Affiliated Oncology Hospital, Guangdong, PR China.

A50 Clinical trials with dianhydrogalactitol (VAL-083) in MGMT-unmethylated glioblastoma. <u>Wang Shen</u>, DelMar Pharmaceuticals, Vancouver, Canada.

Epidemiology

A53 Incidence and Survival Outcomes in Mucinous and Signet-Ring Cell Colorectal Cancers Differ from Classical Adenocarcinoma: A SEER Analysis, 1975-2014. Yaqi Li, Fudan University Shanghai Cancer Center, Shanghai, PR China.

A57 Experimental Copper Depletion Therapy of Prostate Cancer with Tetrathio-molybdate and Bioluminescence imaging. Fang Xie, University of Texas Southwestern Medical Center, Dallas, United States.

A59 Targeting STAT3 Impairs Tumor Invasion and Metastasis through Modulating EZH2/miR-200 Axis in human HNSCC. Xuan Zhou, Tianjin Medical Univ. Cancer Inst. & Hosp., Tianjin, PR China.

A60 Upregulation of PD-L1 in HER2-overexpressing breast cancer cells by trastuzumab through engagement of immune cells and stimulation of IFNgamma secretion. Zhen Fan, UT MD Anderson Cancer Ctr., Houston, United States.

A61 Sodium chloride (NaCl) potentiates digoxin-induced anti-tumor activity in small cell lung cancer. <u>Ke Deng</u>, 1 High Magnetic Field Laboratory, Chinese Academy of Sciences. 2 University of Science and Technology of China, Anhui, PR China.

A62 Drug tolerance regulated by epigenetic memory through branched-chain amino acid metabolic reprogramming. Yuetong Wang, Institute of Biochemistry and Cell Biology Chinese Academy of Sciences, Shanghai, PR China.

A63 Establishment of Kras (G12D)/Trp53 null/Pdx1-cre (KPC) mouse allograft tumor model to facilitate pre-clinical efficacy evaluation of combinatory immunotherapies. Davy Ouyang, Crown Bioscience, Inc., Santa Clara, United States.

A64 MuScreen is a Powerful and Large Scale In Vivo Screening Platform Allowing Efficacy and PD Marker Profiling Using Syngeneic Tumor Models. Lan Zhang, Crown Bioscience, Inc., Santa Clara, United States.

A65 Commensal Microbiota is Involved in Anti-PD-1 mAb-Mediated Anti-Tumor Activity in a Preclinical Tumor Model. Wenging Yang, Crown Bioscience Inc., Santa Clara, United States.

A66 H6, a novel hederagenin derivative, reverses multidrug resistance in vitro and in vivo. Hongbo Wang, Yantai University, Shandong, PR China.

A68 XI-011, a small-molecule inhibitor of MDMX, suppresses cervical cancer cells by activating non-classic p53. Hongbo Wang, Yantai University, Shandong, PR China.

A69 Nanovesicle mediated delivery of anticancer agents effectively regressed intrahepatic tumors in athymic mice. Joseph George, Kanazawa Medical University, Ishikawa, Japan.

Prevention Research

A71 Mobile Mammography Unit Utilization: Perceptions and Interests among African American Women. Marla Hall, East Carolina University, North Carolina, United States.

A72 Inhibiting the specificity protein 1 pathway is involved in dihydroartemisinin-induced caspase-dependent apoptosis in human hepatocellular carcinoma SK-Hep-1 cells. <u>Eunji Im</u>, Kyung Hee University, Seoul, Korea.

A73 Evidence for Indole-3-methyl Isothiocyanate Formation Upon Human Consumption of Brussels Sprouts. Pramod Upadhyaya, University of Minnesota, Minnesota, United States.

A74 3,3'-diindolylmethane triggers endoplasmic reticulum (ER) stress in colorectal cancer cells. <u>Seung Baek</u>, Seoul National University, Seoul, Korea.

A78 BARD1 isoforms are biomarkers for early detection of cancer. <u>Irmgard Irminger-Finger</u>, Univ. of Geneva, Geneva, Switzerland.

Other

A75 Comparison of Tumor 64Cu uptake for Theranostic 64CuCl2-PET/CT Imaging in Copper-depletion Cancer Therapy. Fang Xie, University of Texas Southwestern Medical Center, Dallas, United States.

A76 Exosomes are Potential Novel Mediators for Microbubbles Enhanced Ultrasound Cavitation-Induced Tumor Anti-inflammatory Therapies. Qian Yang, Xijing Hospital, Xi'an, PR China.

A79 Effective miniaturization of small whole genome Next Generation Sequencing by utilizing Illumina Nextera XT library preparation and the Labcyte Echo525 Liquid handler. Charline Hsieh, Labcyte Inc., Sunnyvale, United States.

Tumor Biology

A80 The Role of α -Catulin in Lung Cancer Stemness. Mengfan Huang, National Cheng Kung UNiv., Tainan, Taiwan.

A81 Growth-regulated oncogene-α from oral pre-cancer associated fibroblasts mediates tumor progression in oral cancer. Meiyin Ye, National Cheng Kung Univ., Tainan, Taiwan.

A82 MicroRNA-509-3p enhances cisplatin efficacy in ovarian cancer. Chiahao Tung, National Cheng Kung Univ., Tainan, Taiwan.

A83 SCUBE3 regulates cancer stemness in lung cancer. <u>Yiying Wu</u>, Graduate Institute of Clinical Medicine, College of Medicine, National Cheng Kung University, Tainan, Taiwan.

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Poster Session B— Wednesday, November 8, 2017, 1:00-3:30 p.m.

Molecular and Cellular Biology, Genetics

B02 C19orf12 is a mitochondrial localized metastatic promoter required for the balance of reactive oxygen species (ROS) and mitochondria quality control in non-small cell lung cancer (NSCLC). Meng Zhao, Department of Clinical Laboratory, Tianjin Medical University Cancer Institute and Hospital, National Clinical Research Center for Cancer, Key Laboratory of Cancer Prevention and Therapy, Tianjin's Clinical Research Center for Cancer, Tianjin, P.R. China, Tianjin, PR China.

B03 MiR-199a suppresses NSCLC progression by targeting EML4 in vitro and in vivo. Xiaomin Liu, School of Life of Sciences, Shanghai University, Shanghai, PR China.

B05 CDK2 regulates telomeric replication by phosphorylating TRF1. Rong Tan, Center for Molecular Medicine, Xiangya Hospital, Central South University, Hunan, PR China.

B06 A systems-biology approach to the treatment and study of cancer using agarose encapsulated **RENCA cells.** <u>Tina Kuo</u>, The Rogosin Institute, New York, United States.

B07 Identification of genomic aberrations associated with lymph node metastasis in diffuse-type gastric cancer. <u>Dakeun Lee</u>, Ajou University School of Medicine, Suwon, Korea.

B08 Palmitoylation-dependent activation of MC1R prevents melanomagenesis. <u>Rutao Cui</u>, Boston University, Boston, United States.

B10 Mammary myoepithelial cells respond to damage by altering cell fate in vivo. <u>Lindsey Seldin</u>, Vanderbilt University, Nashville, United States.

B11 MicroRNA-23a-mediated Downregulation of ADCY1 Inhibited Mucosal Melanoma Growth and Migration Through cAMP and MAPK Pathway. Meng Ma, Beijing Cancer Hospital, Beijing, PR China.

B12 Analysis of colorectal cancer related genes from blood samples; circulating tumor cells (CTCs) and circulating cell free DNA (ccfDNA). Kohki Takeda, Department of Surgery, Nippon Medical School Hospital, Tokyo, Japan.

B13 In-situ detection and characterization of EGFR and EGFRvIII expression heterogeneity in glioblastoma FFPE tissues. Emily Park, Advanced Cell Diagnostics, Inc., Newark, United States.

B14 Nuclear Smad6 promotes gliomagenesis by negatively regulating PIAS3-mediated STAT3 inhibition. Jian Zou, Center of Clincical Research, Wuxi People's Hospital of Nanjing Medical University, Jiangsu, PR China.

B17 Knockout validation of Rabbit Monoclonals with recombinant technology to cell cycle regulators. Hongyang Pan, Abcam(Hangzhou) plc, Hangzhou, PR China.

B18 Image-Based Analysis of a Human Neurosphere Stem Cell Model for the Evaluation of Potential Neurotoxicants. <u>Dongping Guo</u>, BioTek instrument Inc, Beijing, PR China.

B19 Automated Label-Free Cell Migration Assays using Magnetic 3D Bioprinting. <u>Dongping Guo</u>, BioTek instrument Inc, Beijing, PR China.

Bioinformatics and Systems Biology

B20 Survival analysis for PDX mouse clinical trials. Sheng Guo, Crown Bioscience, Jiangsu, PR China.

B21 Determining combination effects in cell based assays. Jia Xue, Crown Bioscience, Jiangsu, PR China.

B23 Molecular Heterogeneity of Lung Squamous Cell Carcinomas Patient-derived Xenograft and Matched Tumor. Xin Zhao, BGI, Guangdong, PR China.

B24 MICA: mutual information-based clustering analysis and visualization of single-cell RNA-seq data. Jiyang Yu, St. Jude Children's Research Hospital, Memphis, United States.

Tumor Biology

B26 Quantitative Analysis of Angiomotin Like-2 mRNA Changes in Gastric Cancer Tissue and Plasma.<u>Liping Yang</u>, Cancer Research Center Nantong, Tumor Hospital Affiliated to Nantong University, Jiangxi, PR China.

B28 A Correspondence between Expression of Aberrant Protein of Alkaline Sphingomyelinase and CEA in Colorectal Cancer. <u>Liping Yang</u>, Cancer Research Center Nantong, Tumor Hospital Affiliated to Nantong University, Jiangsu, PR China.

B29 Identification of Phenotypically and Functionally Tumor-derived Endothelial Cells Isolated from Primary Human Hepatocellular Carcinoma. <u>Liping Yang</u>, Cancer Research Center Nantong, Tumor Hospital Affiliated to Nantong University, Jiangsu, PR China.

B30 Circular RNAs are Superabundant in Cervical Tumor and Plasma. Shasha Li, Department of Basic Medical Sciences, School of Medicine, Tsinghua University, Beijing, China, Beijing, PR China.

B32 Epigenetic Reprogramming of Tissue-Specific Transcription Promotes Metastasis. Shuaishuai Teng, Tsinghua University, Beijing, PR China.

B35 High expression of FAM83B predicts poor prognosis in patients with pancreatic ductal adenocarcinoma and correlates with cell cycle and cell proliferation. Chaoqin Shen, Shanghai Jiao Tong University School of Medicine Affiliated Renji Hospital, Shanghai, PR China.

B37 Systematic analysis of gene expression pattern in MCF-7 cells with IncRNA IGKV5 overexpressed. Ziyi Fu, Nanjing Medical University, Jiangsu, PR China.

B38 Contradictory Effects of Mitochondria- and Non-mitochondria-targeted Antioxidants on Hepatocarcinogenesis by Altering DNA Repair. Bibo Wang, Eastern Hepatobiliary Surgery Hospital, Shanghai, PR China.

B39 FTO regulates the chemo-radiation resistance of cervical squamous cell carcinoma (CSCC) by targeting β-catenin through mRNA demethylation. Yanyang Wang, General Hospital of Ningxia Medical University, Ningxia, PR China.

B40 Glipizide inhibits breast cancer growth and metastasis in the mouse model of breast cancer complicated with diabetes mellitus. Mengshi Li, Vascular Biology Research Institute, School of Basic Course, Guangdong Pharmaceutical University, Guangzhou, China, Guangdong, PR China.

B42 The Immune-microenvironment Confers Chemoresistance of Colorectal Cancer through Macrophage-derived IL-6. Zhaohui Huang, Wuxi Oncology Institute, Affiliated Hospital of Jiangnan University, Jiangsu, PR China.

B43 miR-192/215-5p act as tumor suppressors and link Crohn's disease and colorectal cancer by targeting triglyceride synthesis and ECM remodeling. <u>Hu Zhao</u>, Fuzhou General Hospital, Xiamen University, Fujian, PR China.

B44 Epstein—Barr virus noncoding RNAs from the extracellular vesicles of nasopharyngeal carcinoma cells promote angiogenesis via TLR3/RIG-I-mediated VCAM-1 expression. Zhi Li, Xiangya Hospital, Central South University, Hunan, PR China.

B46 Understanding the role of pyruvate metabolism in Diffuse Large B-cell Lymphoma. Peng Wei, Biochemistry Department, University of Utah, Salt Lake, United States.

B47 Technology of hTME-3DX Screen and Verify™. Yong Hu, BioDuro, Beijing, PR China.

B48 The Effects of Immune Checkpoint Modulators on the Clinical Course of Patients with Resectable Hepatocellular Carcinoma. Jihyun An, Asan Medical Center, Seoul, Korea.

B51 Characterization of Tumor-infiltrating Lymphocytes in Breast Cancer by Single cell RNA-seq. <u>Guibo</u> <u>Li</u>, BGI-Research, Shenzhen, Guangdong, PR China.

Cancer Chemistry

B53 Buformin inhibits cellular proliferation via inducing cell cycle arrest and increases chemosensitivity in cervical cancer. <u>Ling Chen</u>, Affiliated Hospital of Jiangnan University, Jiangsu, PR China.

B54 Anti-glycan IgG antibodies profiling for colorectal cancer diagnosis using hydrogel microarrays. <u>Aleksei Tikhonov</u>, Engelhardt Institute of Molecular Biology, Russian Academy of Sciences, Moscow, Russia.

B55 Gene Expression Signature-based High-throughput Screening Reveals Function of Ponatinib in Inhibiting Breast Cancer Lung Metastasis. Wei Shao, Tsinghua University, Beijing, PR China.

Experimental and Molecular Therapeutics

B57 The Human Endogenous Retrovirus TROJAN Promotes Triple Negative Breast Cancer Progression and Represents a Potential Therapeutic Target. <u>Xi Jin</u>, Fudan University Shanghai Cancer Center, Shanghai, PR China.

B58 The inhibition of MDM2 by new antagonist APG-115 triggers apoptosis in p53 wild-type cancer cells in both in vitro and in vivo models. Guangfeng Wang, Ascentage Pharma Group Corp, Ltd., Shanghai, PR China.

B59 Establishment of de novo and viral induced B lymphoma PDX models to evaluate efficacy of BTK inhibitor ibrutinib. Davy Ouyang, Crown Bioscience, Inc., Santa Clara, United States.

B60 Targeting the IRE1 α pathway as a potential therapeutic strategy in prostate cancer. <u>Xia Sheng</u>, University of Oslo, Oslo, Norway.

B61 TGFβ1 Promotes Gemcitabine Resistance through Regulating the NPTN-IT1/ILF3/miR-145 Signaling Axis in Bladder Cancer. Xiaojing Huang, Model Animal Research Center of Nanjing University, Jiangsu, PR China.

B62 Assessment of dianhydrogalactitol (VAL-083) in the treatment of chemoresistant solid tumors. Wang Shen, DelMar Pharmaceuticals, Vancouver, Canada.

B63 SH003, a new herbal formula, inhibits lung cancer proliferation via caspase dependent extrinsic apoptosis pathway. Gyuri Lee, Kyung Hee University, Seoul, Korea.

B64 Anti-cancer-effect of SH003 in p53-wild type liver cancers. <u>Heejae Lee</u>, Kyung Hee University, Seoul, Korea.

B65 Valproic acid induces growth arrest and apoptosis in pancreatic cancer cells via simultaneous down-regulation of EGFR, ErbB2 and ErbB3 in a transcription-independent manner. Qun Ren, Fujian

Key Laboratory of Transplant Biology, Fuzhou General Hospital, Xiamen University, Fuzhou, Fujian, China, Fujian, PR China.

B68 Rac1 GTPase as a Therapeutic Target for Breast Cancer. Ying Yan, University of Nebraska Medical Center, Omaha, United States.

B69 Systems biology and functional genomics identifies HDAC6 as a non-oncogene addiction target for inflammatory breast cancer. Jiyang Yu, St. Jude Children's Research Hospital, Memphis, United States.

B70 Identification of Epigenetic Therapeutic Targets by DNA Methylation Inhibitor, SGI-110, in Hepatocellular Carcinoma. Gangning Liang, USC Norris Comprehensive Cancer Ctr., Los Angeles, United States.

B71 A novel image cytometric analysis method for T cell-mediated cytotoxicity of 3D tumor spheroids. Ting Zhang, Nexcelom Bioscience, Shanghai, PR China.

B72 Acquired resistance to EGFR-TKIs promotes immune escape of lung cancer cells by increasing PD-L1 expression. Shunli Peng, Nanfang Hospital, Southern Medical University., Guangdong, PR China.

B73 Efficacy assessment of investigational human OX40 agonistic antibodies with human OX40 knockin mouse model. Davy Ouyang, Crown Bioscience, Inc., Santa Clara, United States.

B74 Development, characterization and optimization of PBMC-humanized mouse tumor models, MixXeno, as valid a platform to evaluate in vivo activities of immune-oncology drug candidates. <u>Lan Zhang</u>, Crown Bioscience, Inc., Santa Clara, United States.

B75 Flow-based phenotyping of tumor-infiltrate immune cells in novel I/O models. Annie An, Crown Bioscience, Santa Clara, United States.

B76 Topical treatment of All-trans Retinoic Acid inhibits murine melanoma partly by promoting CD8+ T cell immunity. Wei Yin, Immunology, Shanghai, PR China.

B77 Fibroblastic FAP promotes intrehepatic cholangiocarcinoma via the enhancement of cancer stemness-promoting effect of MDSC. <u>Yuli Lin</u>, Fudan University, Shanghai, PR China.

B78 CD47 expression predicts efficacy of macrophage mediated phagocytosis of tumor cells. <u>Huajun Yang</u>, Crown Bioscience, Jiangsu, PR China.

B79 Tumor cell-intrinsic expression of immune checkpoint molecules evaluated by RNA in situ hybridization. Na Li, Advanced Cell Diagnostics, Inc., Beijing, PR China.

B80 Pharmacological inhibition of syngeneic murine cancer cell proliferation by checkpoint inhibitors in combination with targeted agents. Chunlan Dong, Crown Bioscience, Jiangsu, PR China.

B81 Multiplex detection of protein biomarkers using the FirePlex® Technology Platform. <u>Tina He</u>, Abcam, Shanghai, PR China.

B82 Anticoagulants and Cancer Mortality in the Finnish Randomized Study of Screening for Prostate
Cancer. Pete Kinnunen, Faculty of Medicine, Tampere, Finland.