1. From the Editors

From the Editors, with Dr. Terry Moore, Editorial Board Member

Each quarter the Editorial Board selects an area to highlight from the broad range of topics that fall under the umbrella of Chemistry in Cancer Research. Our topic this quarter is Targeting Transcription in Cancer. Editorial Board member Dr. Terry Moore has taken the lead in assembling an overview of the topic.

TARGETING TRANSCRIPTION IN CANCER

As recently as a decade ago, it would have been argued that transcriptional pathways provided few druggable targets. Part of the reasoning behind this is that many transcription factors exhibit relatively simple and ubiquitous structural elements that provide for poor small molecule binding sites; however, because aberrantly regulated transcriptional networks are a hallmark of many cancers, the rationale for targeting transcription is compelling in many cases, and there have been many recent advances that demonstrate the utility of targeting transcription in cancer. We've dedicated this issue to examining this topic.
Several strategies have been employed to affect transcription in cancer. The first and most obvious is to directly target transcription factors themselves. This approach has largely been limited to the ligand-binding domains of nuclear receptors. Some orphan nuclear receptors (e.g., Rev-ERb, SHP, etc.) represent important recent targets, but there continues to be interest in many classic targets (e.g., estrogen receptor, androgen receptor), which arguably formed the foundation of targeted cancer therapy in the 1970s. The second approach involves binding of small molecules to regulatory proteins. This is perhaps best typified by the efforts to inhibit the interaction of p53 with its ubiquitin ligase partner HDM2, resulting in several clinical trials for lymphoma and leukemia. More recently, there has been interest in inhibiting regulatory proteins in the Nrf2 and NF-κB pathways for chemoprevention and chemotherapy, respectively. Also included in this category would be the substantial efforts that have been invested in targeting epigenetic regulators, like BRD4, that interact with modified chromatin to regulate transcription. These efforts have led to several clinical candidates. The final approach involves developing small molecules that directly bind to DNA, rather than to transcription factors, cofactors, regulatory proteins or other transcription machinery elements. The most well-developed examples of these types of molecules are the pyrrole-imidazole polyamides, developed by Dr. Peter Dervan's lab.

Coupling an increased understanding of transcriptional pathways with enabling technologies will yield an even greater focus on targeting transcription in cancer in coming years. New technologies include CRISPR/Cas9, proteolysis targeting chimeras (PROTACs), and a slew of recently solved x-ray crystal structures of components of the transcription machinery. One of the developers of new technologies for studying these potential drug targets is Dr. William Pomerantz,

an assistant professor of chemistry at the University of Minnesota and the subject of this issue's Early Career Scientist profile. Dr. Pomerantz develops new NMR methods for studying transcription factors and epigenetic regulators, and one of his recent papers on PrOF NMR is covered in this issue's Research Highlights.

2017 AACR National Meeting, April 1-5 2017, Washington, DC

The 2017 AACR Annual Meeting is only weeks away. For those CICR members attending, a listing of CICR-sponsored sessions can be viewed on the CICR at the Annual Meeting page (insert link) once the program is finalized. Among the highlights are the "From Chemistry to the Clinic: Pathways for Drug Discovery and Development" educational sessions on Saturday, April 1 and the "New Drugs on the Horizon" session on Sunday, April 2. Note that the CICR Town Hall meeting will immediately follow this session, in the same room. We encourage you to stay, enjoy a refreshment, network and learn more about your CICR before heading out for dinner. The program will include updates on current and planned CICR initiatives and a Q&A session with the CICR leadership. Newsletter Editorial Board members will also be present, and we would be happy to hear your input on how to make this newsletter valuable for all CICR members.

CICR Town Hall Meeting (*Refreshments provided*)
Sunday, April 2, 2017
6:30-8:00 p.m. (immediately following the *New Drugs on the Horizon* session, being held in the same location)
Walter E. Washington Convention Center, East Hall, Salon AB

Another opportunity for those attending the Annual Meeting is the Cancer and Biomedical Research Career Fair on Saturday April1, 9:00-3:00. (See CancerCareers.org for details, registration for job seekers is free.) If you plan to participate, check the Career Forum section of the newsletter for some tips on getting the most out of a Job Fair.

Finally, the Editorial Board would like to recognize and thank our immediate Past Editor, Dr. Klaus Pors for his service to the CICR. He has played a big role in upgrading the newsletter and has set a high standard that we hope to continue to build upon in the coming year.

2. Selected Research Highlights

Review Article
"The Structural Basis of Transcription: 10 Years After the Nobel Prize in Chemistry"
Merle Hantsche and Patrick Cramer
Angewandte Chemie International Edition, **2016,** *55,* 15972-15981. doi: 10.1002/anie.201608066
http://onlinelibrary.wiley.com/doi/10.1002/anie.201608066/epdf

This minireview provides an overview of the current understanding of the structural basis of eukaryotic gene transcription and how that understanding has evolved over the last decade.

"Protein-Observed Fluorine NMR Is a Complementary Ligand Discovery Method to 1H CPMG Ligand-Observed NMR"
Andrew K. Urick, Luis Pablo Calle, Juan F. Espinosa, Haitao Hu and William C. K. Pomerantz
ACS Chemical Biology, 2016, 11, 3154-3164. DOI:
10.1021/acschembio.6b00730
http://pubs.acs.org/doi/abs/10.1021/acschembio.6b00730
A collaboration between scientists at Eli Lilly and Company and the Pomerantz lab at the University of Minnesota undertook a systematic comparison of Protein-Observed Fluorine NMR (PrOF) vs Proton CPMG Ligand observed NMR as techniques for fragment screening. For comparison, a set of 930 fragment molecules was screened as mixtures of 5 for binding to the first bromodomain of BRD4 as the protein target with each technique. The PrOF technique used BRD4 BDI protein with 5-F tryptophan incorporated at all three W sites in the protein fragment and monitored perturbations on the ^{19}F signals on fragment binding for detection. Good agreement was seen in the results for the two techniques. The authors conclude that the tools are quite similar in their detection abilities for this protein target. The choice of which technique to use may be protein-dependent, with factors such as availability of reference compounds, protein size and expression efficiency and multiple binding sites influencing the decision.

"Discovery of a Chemical Probe Bisamide (CCT251236): An Orally Bioavailable Efficacious Pirin Ligand from a Heat Shock Transcription Factor 1 (HSF1) Phenotypic Screen"
Matthew D. Cheeseman, Nicola E. A. Chessum, Carl S. Rye, A. Elisa Pasqua, Michael J. Tucker, Birgit Wilding, Lindsay E. Evans, Susan Lepri, Meirion Richards, Swee Y. Sharp, Salyha Ali, Martin Rowlands, Lisa O'Fee, Asadh Miah, Angela Hayes, Alan T. Henley, Marissa Powers, Robert te Poele, Emmanuel De Billy, Loredana Pellegrino, Florence Raynaud, Rosemary Burke, Rob L. M. van Montfort, Suzanne A. Eccles, Paul Workman, and Keith Jones
Journal of Medicinal Chemistry, **2016,** ASAP.
http://pubs.acs.org/doi/abs/10.1021/acs.jmedchem.6b01055
Cheeseman et al. describe a novel chemical probe that inhibits the Heat Shock Transcription Factor 1 (HSF-1)-mediated stress pathway. Inhibiting the HSF-1 pathway could lead to a viable cancer therapeutic, as aberrant activation of HSF-1 has been shown to lead to tumorigenesis and adverse clinical outcomes. After carrying out a phenotypic screen, the authors describe optimization of a bisamide with nanomolar cellular potency in an ovarian carcinoma cell line (SK-OV-3). The compound displays good mouse pharmacokinetic properties and shows efficacy at 20 mg/kg p.o. in an ovarian cancer tumor xenograft model. The authors carried out chemoproteomic target identification, SPR, and x-ray crystallography studies

to confirm that the target of the molecule is pirin, a putative regulator of transcription factors, including HSF-1.

"A Synthetic Loop Replacement Peptide That Blocks Canonical NF-κB Signaling"
Paul A. Bruno, Alex Morriss-Andrews, Andrew R. Henderson, Charles L. Brooks III, Anna K. Mapp
Angewandte Chemie International Edition, **2016**, *55*, 14997.
http://onlinelibrary.wiley.com/doi/10.1002/anie.201607990/full
Because of its role in regulating the expression of tumor-promoting cytokines, the transcription factor NF-κB is thought to be a critical link between cancer and inflammation. As such, there is significant interest in developing selective inhibitors of NF-κB. Bruno et al. describe a macrocyclic peptide that blocks canonical NF-κB signaling by blocking the interaction of two upstream regulatory proteins in the NF-κB signaling pathway: NEMO and IKK. The authors use ring-closing metathesis to recapitulate a key hydrogen bond formed between serine and aspartate in an LDWSWL sequence derived from the two isoforms (α and β) of IKK. The macrocycle demonstrates higher potency and proteolytic stability than the native peptide and may provide a general framework for other protein-protein interactions with similar structural motifs.

"RNA polymerase II sense obstruction in the DNA minor groove via a conserved sensor motif"
Liang Xu, Wei Wang, Deanna Gotte, Fei Yang, Alissa A. Hare, Timothy R. Welch, Benjamin C. Li, Ji Hyun Shin, Jenny Chong, Jeffrey N. Strathern, Peter B. Dervan, and Dong Wang
Proceedings of the National Academy of Sciences, **2016,** *113*, 12426.
http://www.pnas.org/content/113/44/12426.abstract

Developed in the Dervan Lab at Caltech, pyrrole-imidazole (Py-Im) polyamides are small molecules designed to interact with specific sequences in the minor groove of DNA. While cell-permeable Py-Im polyamides have been shown to regulate transcription in several different systems, the mechanisms by which they prevent RNA polymerase II-mediated elongation are not fully understood. Xu et al. shed light on this problem by demonstrating that two residues (His1386 and Arg1387) in the Switch 1 region of RNA polymerase II serve as sensor residues that can detect Py-Im polyamides bound to the minor groove. Detection of a polyamide causes RNA polymerase II to stall on the DNA for more than 20 hours and is resistant, perhaps by slow polyamide dissociation, to some of the repair processes that RNA polymerase II might routinely encounter

Proteome Profiling Outperforms Transcriptome Profiling for Coexpression Based Gene Function Prediction
https://www.ncbi.nlm.nih.gov/pubmed/27836980
Profiling of mRNA is commonly performed to assess gene expression and elucidate cellular function, with the coexpression of mRNAS under various conditions presumed to be linked to cofunctionality – using approaches such as clustering, gene set enrichment analysis, and network analysis. A number of

studies have suggested discrepancies at the gene expression and protein expression often do not correlate, possibly due to a number of factors. In a recent report, Wang et al. sought to systematically assess whether the protein expression profiling provided by recent developments in mass spectrometry-based proteomic technologies would be capable of outperforming transcriptome profiling for gene function prediction based on coexpression. Matched mRNA and protein expression data for three different cancer types was obtained from The Cancer Genome Atlas and the Clinical Proteomic Tumor Analysis Consortium and used to construct mRNA and protein coexpression networks. Notable differences were observed in the types of connectivity between the mRNA and protein coexpression networks. Interestingly coexpression of proteins was dominated by functional similarity, whereas mRNA coexpression was dominated by both cofunction and chromosomal colocalization. The authors further demonstrated that protein level data helped strengthen the link between gene expression and function for a significant percentage of Gene Ontology biological process and KEGG pathways. Also of interest, novel relationships between gene and function were revealed including between HER2 and lipid biosynthetic process in breast cancer, identification of a new gene in complement activation, and identification of a new epithelial-to-mesenchymal transition marker. This study suggests that protein level data may outperform mRNA expression data for gene function prediction based on coexpression and proteomic analysis should be an integral part of gene function and human disease studies.
Mol Cell Proteomics. 2017 Jan;16(1):121-134. doi: 10.1074/mcp.M116.060301. Epub 2016 Nov 11.

Somatic mutation detection using various targeted detection assays in paired samples of circulating tumor DNA, primary tumor and metastases from patients undergoing resection of colorectal liver metastases.
https://www.ncbi.nlm.nih.gov/pubmed/28029553
Recently, circulating tumor DNA (ctDNA) has emerged as a promising and minimally invasive means of monitoring patient tumor behavior. Despite the promise of this approach, there are numerous benchmarking studies that remain to fully vet and understand the measurements and information that can be provided by ctDNA, such remote detection of somatic mutations from the tumor. Beije et al. have recently reported a study to detect somatic mutations using various assays in paired samples of primary tumor, metastatic liver tissue, normal tumor-adjacent colon or liver tissue and whole blood from 12 metastatic colorectal cancer patients undergoing resection of liver metastases. These samples were analyzed to assess the feasibility of a targeted next generation sequencing (NGS) approach to identify somatic mutations in cell free DNA (cfDNA) isolated from whole blood. This approach was further compared with the OnTarget assay, and with digital PCR (dPCR). Sequencing of 21 colorectal cancer specific genes was performed on tissues and cfDNA samples. cfDNA and DNA extracted from whole blood and normal tissue were analyzed by the OnTarget assay and dPCR for specific mutations detected in the matched

primary and/or metastatic tumor tissue. Various comparisons were made between the NGS data and the OnTarget and dPCR data. The authors concluded that NGS on cfDNA was feasible but the sensitivity of the method to detect all somatic mutations present in tissue was limited. However, dPCR and enrichment of mutant allelles prior to NGS increased sensitivity in somatic mutation detection.
Mol Oncol. 2016 Oct 10. pii: S1574-7891(16)30110-7. doi: 10.1016/j.molonc.2016.10.001. [Epub ahead of print]

Plasma Circulating Tumor DNA in Pancreatic Cancer Patients Is a Prognostic Marker.
https://www.ncbi.nlm.nih.gov/pubmed/27993964
Pancreatic cancer is a leading cause of cancer-related deaths and prognosis of the disease remains poor. Circulating tumor DNA (ctDNA) present in blood presents a promising and non-invasive alternative to analysis of tumor tissue. In a recent study Pietrasz et al. sought to assess the feasibility and prognostic value of ctDNA in pancreatic cancer. Prospective blood samples collected over four years were obtained from patients being treated for pancreatic cancer. Next generation sequencing (NGS) and digital PCR (dPCR) were used to measure mutations specific for pancreatic cancer. 48% of advanced pancreatic cancer patients had ctDNA detected with a median threshold frequency and the detection was highly correlated with poor overall survival. In addition, patients were grouped according to the frequency of their mutations. Overall the presence of ctDNA was associated with shorter-free survival and shorter overall survival. This study suggests that ctDNA may have a role in advanced pancreatic cancer prognostication, and as an indicator of shorter disease-free survival in resected patients if detected after surgery.

Clin Cancer Res. 2017 Jan 1;23(1):116-123. doi: 10.1158/1078-0432.CCR-16-0806. Epub 2016 Dec 19.

The MCL1 inhibitor S63845 is tolerable and effective in diverse cancer models.

Kotschy, A.; Szlavik, Z.; Murray, J.; Davidson, J.; Maragno, A. L.; Le Toumelin-Braizat, G.; Chanrion, M.; Kelly, G. L.; Gong, J.-N.; Moujalled, D. M.; Bruno, A.; Csekei, M.; Paczal, A.; Szabo, Z. B.; Sipos, S.; Radics, G.; Proszenyak, A.; Balint, B.; Ondi, L.; Blasko, G.; Robertson, A.; Surgenor, A.; Dokurno, P.; Chen, I.; Matassova, N.; Smith, J.; Pedder, C.; Graham, C.; Studeny, A.; Lysiak-Auvity, G.; Girard, A.-M.; Gravé, F.; Segal, D.; Riffkin, C. D.; Pomilio, G.; Galbraith, L. C. A.; Aubrey, B. J.; Brennan, M. S.; Herold, M. J.; Chang, C.; Guasconi, G.; Cauquil, N.; Melchiore, F.; Guigal-Stephan, N.; Lockhart, B.; Colland, F.; Hickman, J. A.; Roberts, A. W.; Huang, D. C. S.; Wei, A. H.; Strasser, A.; Lessene, G.; Geneste, O.

Nature, **2016**, *538*(7626), 477–482. DOI: 10.1038/nature19830.

A new potent and selective small-molecule inhibitor of MCL1 is described. The compound, S63845, has *in vitro* and *in vivo* activity in MCL1 dependent cell lines. The compound was applied to a number of solid tumor models and showed activity as a mono-agent and in combination with oncogenic kinases. The MCL1 inhibitor was shown to induce functional signals of apoptosis and kill cells in a BAX/BAK dependent manner. The study provides preclinical evidence that targeting MCL1 with a BH3 mimetic small molecule drug results in a robust anti-cancer response and that MCL1 is a druggable target.

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hBfl-1/hNOXA Interaction Studies Provide New Insights on the Role of Bfl-1 in Cancer Cell Resistance and for the Design of Novel Anticancer Agents.

Barile, E.; Marconi, G. D.; De, S. K.; Baggio, C.; Gambini, L.; Salem, A. F.; Kashyap, M. K.; Castro, J. E.; Kipps, T. J.; Pellecchia, M.

ACS Chem. Biol. **2016**, ASAP. DOI: 10.1021/acschembio.6b00962.

Both Mcl-1 and Bfl-1 are known to interact with pro-apoptotic NOXA. Although studies using mouse proteins indicated that Mcl-1 interacts tightly with NOXA, Barile et al have found using human proteins, that hBfl-1 has the highest affinity for hNOXA. This difference between the affinity of the mouse and human proteins was structurally linked to a unique disulfide bond that results between hBfl-1 and hNOXA on binding, due to the presence of cysteine residues in both human proteins. This covalent interaction is not seen in other antiapoptotic Bcl-2 proteins, including mouse Bfl-1, or in other BH3 peptides. The data focuses attention on Bfl-1 as a drug target and suggests that the cysteine residues provide a handle for the development of covalent inhibitors of this protein.

PI3Kγ is a molecular switch that controls immune suppression.

Kaneda, M. M.; Messer, K. S.; Ralainirina, N.; Li, H.; Leem, C.; Gorjestani, S.; Woo, G.; Nguyen, A. V.; Figueiredo, C. C.; Foubert, P.; Schmid, M. C.; Pink, M.; Winkler, D. G.; Rausch, M.; Palombella, V. J.; Kutok, J.; McGovern, K.; Frazer, K. A.; Wu, X.; Karin, M.; Sasik, R.; Cohen, E. E. W.; Varner, J. A.Kaneda, M. M. et al.

Nature, **2016**, 539, 437–442. DOI: 10.1038/nature19834.

Overcoming resistance to checkpoint blockade therapy by targeting PI3Kγ in myeloid cells.

De Henau, O.; Rausch, M.; Winkler, D.; Campesato, L. F.; Liu, C.; Cymerman, D. H.; Budhu, S.; Ghosh, A.; Pink, M.; Tchaicha, J.; Douglas, M.; Tibbitts, T.; Sharma, S.; Proctor, J.; Kosmider, N.; White, K.; Stern, H.; Soglia, J.; Adams, J.; Palombella, V. J.; McGovern, K.; Kutok, J. L.; Wolchok, J. D.; Merghoub, T.

Nature, **2016**, 539, 443–447. DOI: 10.1038/nature20554.

These two papers show that targeting PI3Kγ in myeloid cells can reduce immune suppression and increase the efficacy of immune checkpoint inhibitors. De Henau et al. found that checkpoint blockade resistant tumor models had increased infiltration of immunosuppressive myeloid cells. Linking the known high expression and mechanistic importance of PI3Kγ in myeloid cells, the authors tested a selective inhibitor (IPI-549) of the isoform to test whether this would re-sensitize resistant tumor models. Kaneda et al found that mice lacking PI3Kγ and mice treated with PI3Kγ antagonists suppressed growth of their implanted tumors. The authors linked inhibition of PI3Kγ to the enhanced expression of various immune-activators and the reduction of immune-suppressors. In both papers, combinations of PDL1 or CTLA4 inhibitors with a PI3Kγ inhibitor improved antitumor efficacy. These results offer the chance that combinations of this type may be efficacious against resistant tumors which have high infiltration of immunosuppressive myeloid cells.

3. Profile of an Early-career Researcher: Prof. William Pomerantz

Prof. William Pomerantz is an assistant professor of chemistry at the University of Minnesota. He obtained a Bachelor's degree in chemistry from Ithaca College in 2002. From 2002-2003, he studied under Professor François Diederich and Professor Emeritus Jack Dunitz at the Swiss Federal Institute of Technology, (ETH, Zürich) under a Seydel/Fulbright Fellowship. With the guidance of Prof. Samuel Gellman and Prof. Nick Abbott, he graduated with his Ph.D. in chemistry from the University of Wisconsin-Madison in 2008, where he worked on biophysical studies of rationally designed β-peptides and their higher-ordered assemblies. From 2009-2012, he studied molecular interactions of transcription factor complexes on an NIH NRSA postdoctoral fellowship with Prof. Anna Mapp at the University of Michigan. He started his independent lab at the University of Minnesota in 2012.

Prof. Pomerantz's research program develops new chemistry- and structure-based discovery approaches to study protein-protein interactions (PPIs) implicated in cancer and heart disease. His lab applies NMR and MRI to visualize biomolecular interactions and uses novel small molecules to perturb protein function. His recent focus is in the area of fragment-based ligand discovery applied to the field of epigenetics. One method developed in his lab employs metabolic labeling of proteins with fluorinated amino acids for use in protein-based ^{19}F NMR small molecule screens. His lab uses ^{19}F NMR to determine how a molecule interacts at a protein surface to inform the use of chemistry to design new molecules with more potent activity. His lab recently used this approach to discover the first small molecule inhibitors of BPTF (Bromodomain PHD Finger Transcription Factor) to understand its role in regulating transcription in cancer, and is currently following up on the role of this protein in regulating the oncogenic protein, c-Myc.

His lab's research and educational goals have been recognized by an NSF CAREER award, Cottrell Research Scholar Award, and a recent designation as a "rising star in chemical biology" by the International Chemical Biology Society. His laboratory's research using ^{19}F NMR has attracted attention in both academic and industrial settings, leading to collaborations with researchers at the University of Minnesota, the Moffitt Cancer Center, Cold Spring Harbor, Eli Lilly, and others. Prof. Pomerantz is an author of 31 research articles. His lab has attracted funding from the National Institutes of Health, the National Science Foundation, the Research Corporation, the American Cancer Society, the Sidney Kimmel Cancer foundation, the Masonic Cancer Center, the American Heart Association, and Eli Lilly.

4. Spotlight on World News

President Barack Obama signs the 21st Century Cures Act into law
In December, President Barack Obama signed the 21st Century Cures Act into law. Among the many provisions are $1.8 billion in funding for the cancer research "moonshot" initiative and authorization of $1 billion in funding to state programs to treat and prevent the abuse of heroin, other opioids and addictive drugs over two years. The measure overall calls for $6.3 billion in new spending in the next 10 years, although the future funding authorizations will require additional legislative action. The full text of the act can be found at this URL: https://www.congress.gov/114/bills/hr6/BILLS-114hr6rfs.pdf.

The act also includes provisions related to the FDA review process for Drugs and Devices (See Title II in the document) including Patient-Focused Drug Development, Modern Trial Design and use of Real World Evidence in the approval process. How these provisions will be put in to practice will have major implications for the development of new cancer treatments. A recent article in the New England Journal of Medicine (N Engl J Med 2016; 375:2293-2297, DOI: 10.1056/NEJMsb1609216) and blog posting (http://blogs.fda.gov/fdavoice/index.php/2016/12/21st-century-cures-act-making-progress-on-shared-goals-for-patients) offer some insight in to how FDA leaders view the use of Real World Evidence.

PD-L1 antibody second line use for NSCLC endorsed by NICE
The UK's NICE new draft guidelines endorsed the use of Merck Sharp & Dohme's Keytruda (pembrolizumab) to treat locally advanced or metastatic PD-L1-positive non-small cell lung cancer in adults who have had at least one round of chemotherapy. The guidelines stipulated that treatment with Keytruda be stopped at two years of uninterrupted treatment and no documented disease progression, and that MSD should continue to provide the drug at the discount agreed in the new patient access scheme. "If companies work with us to price drugs reasonably and manage any uncertainties in the evidence base, we can continue to recommend patients have routine access to the treatments they

need," said Carole Longson, director of the NICE center for health technology evaluation. Earlier draft guidance had found the agent not cost-effective at list price.
Source: Pharmaphorum

Antibody Drug Conjugate Adcentris considered non-cost effective for Hodgkin's Lymphoma by NICE
The UK's NICE concluded there was substantial uncertainty in the clinical evidence and agreed that Takeda Pharmaceutical's Adcetris (brentuximab vedotin) could not be considered a cost-effective use of National Health Service resources for Hodgkin lymphoma. Adcetris is cleared for CD30-positive Hodgkin lymphoma patients in Europe with relapsed or refractory Hodgkin's lymphoma after autologous stem cell transplant, a high risk of disease relapse or progression, and relapsed or refractory disease after two previous therapies when autologous stem cell transplant or multi-agent chemotherapy is not an option.
Source: Pharmaphorum

5. News from the CICR Steering Committee

The CICR Steering Committee has four subgroups working behind the scenes to advance the four initiatives adopted by the 2016-17 CICR Steering Committee. Progress has been made on each as described below.

Chemical Probes subgroup
Under David Uehling's leadership, the Chemical Probes subgroup has expanded its membership to include diverse representation from academic, industry and government not-for-profit institutions. With the goal of educating the Cancer Research community as to the optimal use of chemical probes, the Working Group held a teleconference discussion on December 14 to further enhance the CICR Resources webpage in order to promote effective dissemination of information on chemical probes in research. As a result, the site has been updated to include the specific expertise of CICR contacts willing to provide guidance to cancer researchers, a list of probes that are frequently misused in cancer research, and additional references and links for the cancer research community as a whole.

Outreach subgroup
Melissa Vasbinder is leading the CICR Outreach subgroup whose mission is to promote cancer chemistry research by providing opportunities to connect chemists, network, and share science. The objective for 2016-17 has been focused on increasing geographic diversity within CICR, specifically in Asia and Europe and ensuring that CICR members have opportunities to connect with chemists outside of the annual AACR meetings. A proposal for a joint ACS/AACR symposium is being generated that would provide an additional venue for

chemists to meet and share science. The joint symposium will be formatted to facilitate scientific exchange, akin to Gordon Research Conferences.

Development of next-generation of chemists in cancer drug discovery subgroup

A third CICR Working Group is focused on promoting the development of the next-generation of chemists in cancer drug discovery and is being led by Sean Kerwin. This team seeks to identify the challenges to maintaining a flow of top-notch chemists engaged in cancer research and identify mechanisms to facilitate the training and transitioning of chemists to careers in oncology research by engaging academic, industry, and research institute stakeholders. The Working Group's initial focus is to facilitate these efforts through networking sessions in which stakeholders can share information and ideas and identify actionable items that CICR can pursue to improve support for next-generation chemists.

Connecting academic and industrial researchers in cancer drug discovery subgroup

A related Working Group seeks to solidify the connection between researchers doing cancer drug discovery in industry and academic settings and is being led by Vinod Patel. Collaboration between industry and academia has proven a fruitful approach to enhancing success in oncology drug discovery, one recent example being the discovery of the prostate cancer drug Xtandi, by Medivation in collaboration with academic researchers at UCLA. The CICR Working Group seeks to build on this type of success by providing simple and user-friendly tools for practitioners of drug discovery in academia, government/private institutes and industry to connect, and collaborate. Specific goals are focused on 1) collating a comprehensive directory of academic labs engaged in cancer drug discovery, 2) building a readily searchable directory on the website and 3), creating a site with information on "best practices" for academia-industry collaboration . A summary of the output from all four Working Groups will be presented at the CICR Town Hall meeting at the AACR Annual Meeting in early April. CICR members interested in contributing to any of the Working Groups are encouraged to contact the leaders listed below:

Dr. David Uehling, Ontario Institute of Cancer Research:
daviduehling@gmail.com
Dr. Melissa Vasbinder, Ribon Therapeutics: mvasbinder@ribontx.com
Dr. Sean Kerwin, Texas State University: smk89@txstate.edu
Dr. Vinod Patel, APC Therapeutics: vinodfpatel@apctherapeutic.com

6. Career Forum

https://cancercareers.org/Pages/default.aspx

Cancer and Biomedical Research Career Fair,
AACR National Meeting, Washington, DC, Saturday April1

See CancerCareers.org for details and registration, registration for job seekers is free.

Participating in a large Career Fair can be a daunting experience. To help you get the most out of participating, the editors solicited advice from Annie Tomczyk, Manager, R&D Executive Search at AbbVie, Inc. and veteran of recruiting at many Career Fairs at large scientific meetings.

An internet search on Job Fairs or Career Fairs will turn up numerous articles offering useful advice; however, few of the items focus specifically on the sciences. One item from *Science* which does (http://www.sciencemag.org/careers/2005/12/making-most-career-fairs) is useful, but is a bit dated in terms of integrating the internet and your online presence in your job search. Here are some tips to get the most out of participating in the Cancer and Biomedical Research Career Fair and similar career fairs associated with large scientific meetings.

- Do your homework! Walk in to the hall with a list of the companies you are interested in. Focus on 3-5 that look like a good match rather than spamming your CV to every booth in the place.
- Search the positions posted ahead of time to identify openings that could be right for you. Be realistic about whether your experience matches any criteria listed. If your qualifications are not explicitly stated in your CV, take the initiative and point out your relevant experiences. Remember that the recruiter may not be an expert in your field, so help them make the connections between your experiences and the criteria in the job posting. Be able to articulate how both the position and the company are a good fit for you.
- When you step up to a career booth, be prepared to identify your focus. Have some knowledge of the company and the openings they have posted as mentioned above. Approach with confidence and introduce yourself, don't just hand over your CV. Think through the messaging you want to portray to the recruiter (or possibly business leader) you interact with. Consider asking some questions that will show you are seriously considering the company, but avoid things that you could have (and should have!) already found on the company web page. Questions about the company culture show your interest, and more importantly help you decide if the company is the right fit for you.
- Take advantage of the fact that the Career Fair is part of a major scientific conference. Search the conference abstracts for presentations by scientists from the companies you are interested in. This is a great chance to learn about the company's science. If you are a LinkedIn member (you should be if you are looking for a job!), request to meet company scientists participating in the conference (if there is an attendee list available) who work in your area of expertise. You might have a chance to talk to them at the end of a session, or at their poster if they are

giving one. If you do, be prepared. Have a question or two ready and be prepared to talk about your science.

- Remember that your search doesn't start or end with the Career Fair. Make use of the resources available to you, including the internet. Use resources like LinkedIn; if you invest some time you can find a lot of great information there. Another good source is Forbes, they have a lot of timely features related to careers and professional growth. Spend some time on your LinkedIn profile to make sure it fully reflects your experiences and professional interests. Chances are that at some point in the interview process someone involved in assessing you (recruiter, hiring manager, people on your interview schedule) will look at your profile.

Additional job postings:

http://www.nature.com/naturejobs/science/jobs

http://jobs.rsc.org/

http://chemistryjobs.acs.org/

7. Conferences

AACR Annual Meeting 2017
April 1-5, 2017, Washington, D.C.
Web Site

Royal Society of Chemistry Fragments 2017
March 5-7, Vienna Austria
Website

253rd ACS National Meeting & Exposition
April 2-6, 2017, San Francisco, California
Web Site

Cambridge Healthtech Institute Drug Discovery Chemistry Conference
April 24-27, San Diego, CA
http://www.drugdiscoverychemistry.com/

100th Canadian Chemistry Conference and Exhibition
May 28 to June 1, 2017, Toronto, Ontario, Canada
Web Site

NovAliX Biophysics in Drug Discovery
June 6-9, Strasborg, France
Website

Bioorganic Gordon Research Conference
June 11-16, 2017, Andover, NH
https://www.grc.org/programs.aspx?id=12319

American Peptide Society Meeting
http://aps2017.org
June 17-22, 2017. Whistler, BC, Canada

ACS MEDI-EFMC: Medicinal Chemistry Frontiers 2017
June 25-28, 2017, Philadelphia, Pennsylvania
Web Site

Royal Australian Chemical Institute Centenary Congress
July 23-28, Melbourne, Australia
Website

Gordon Research Conference in Medicinal Chemistry 2017
August 6-11, 2017, New London, NH
Web Site

254th ACS National Meeting & Exposition
August 20-24, 2017, Washington, DC

EFMC-ASMC'17 European Federation for Medicinal Chemistry International Symposium on Advances in Synthetic and Medicinal Chemistry
August 27-31, 2017, Vienna, Austria
www.efmc-asmc.org/

AACR-NCI-EORTC Molecular Targets and Cancer Therapeutics
October 26-30, 2017, Philadelphia, Pennsylvania
Web Site