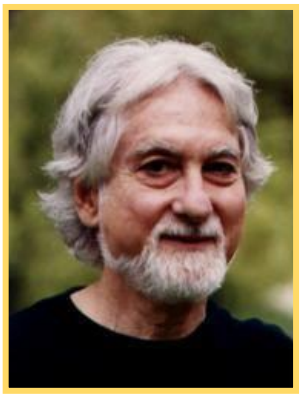
JURA
Journal of Undergraduate Research in Alberta • Volume 6 • 2017

University of Calgary Faculty Interviews

All great researchers were a novice at some point. The JURA editors have caught up with a few of the great researchers at the University of Calgary to get some insight on their experience writing their 1st first-author publication.



Morley D Hollenberg,
BSc, MSc, PhD, MD
Research interests: Proteinase activated receptors (a type of G-protein coupled receptors) in human disease

Wallace K. MacNaughton,
BSc, MSc, PhD
Research Interests: Gastrointestinal inflammation and epithelial biology

Mark Ungrin,
BSc, PhD
Research interests: Micro-tissue engineering focused on diabetes treaments and macular degeneration

1 JURA: What was the topic of your first published, scientific article and was it related to your current field of study?

MH: My first-authored paper written entirely by me along with my supervisor was data coming from my thesis work. The published topic was the isolation of the multiple oxytocin-vasopressin 'neurophysin' binding proteins from the posterior pituitary gland.

WM: My first first-author paper came out of my MSc work, and involved a study of how mild irritation of the gastric mucosa could confer protection against a subsequent damaging challenge. I still study the gastrointestinal mucosa, so you could say that this was the publication that got me started on a research area that I'm still interested in 30 years later.

MU: Working at Merck-Frosst, I had developed a medium-throughput assay for the activation of certain cell surface receptors, and used it to assess activation of the human EP1 prostanoid receptor. It was not initially related to what we are working on now, but this experience caused me to ask certain questions in our current research, and it looks like we will get at least one paper out of the resulting findings.

2 **JURA: Did your first submission get accepted, require revisions, or get rejected? If rejected, how many attempts did it take until the manuscript was accepted?**

MH: My first submission was accepted with suggestions for revisions. Both manuscripts accepted after revision x 1.

WM: This is a difficult question, because it was so long ago and my supervisor was the corresponding author. As I recall, the manuscript was accepted with revisions. We didn't have to do any extra experiments, so it was accepted rather quickly upon resubmission.

MU: The initial submission was rejected emphatically. Not only did they not like the paper, they questioned why anyone would have wanted to do the work in the first place! In retrospect we had sent it to the wrong journal for the nature of the work, but at the time it was very discouraging. We then sent it somewhere else (Analytical Biochemistry) and it was accepted with very positive reviews and only minor changes requested. The paper has now been cited 57 times and the assay has been used at several Merck sites internationally, and shows up in several patents.

3 **JURA: Looking back, what was the most important skill you learned or improved while writing and publishing your first scientific article?**

MH: The writing skills learned were sitting with my supervisor/collaborator, sketching out the manuscript first; then doing iterative editing, going back/forth between supervisor/collaborators. Persistence in generating a revision responding to the reviewers' critique.

WM: I think I learned three important things when working on my first manuscript. First, you have to tell a compelling story. Just reporting data isn't enough – you have to make it interesting. Second, you need to show the relevance of your work. In biomedical science this means demonstrating clearly how your work is of clinical importance. Third, you have to be honest – don't cut corners and don't publish anything that you don't believe in 100%. These are still important to me in papers I publish now.

MU: It's very important to identify an audience that is predisposed to understand why your work matters; and then to explain clearly what makes it important. The best science in the world, if poorly presented, may not have much impact because no-one pays attention to it. Even though you know how big the potential impact of your work is, that doesn't mean it's as obvious as you think to everyone else.

4 **JURA: What is the main difference in the way you wrote your first scientific article and an article you would write today?**

MH: Today, I sit with my trainees to sketch the manuscript; then let them do the first draft on their own, followed by iterative edits involving all collaborators.

WM: Most articles I write today are actually written by trainees in my lab. My job is to provide oversight and pointers to help grad students and postdocs learn the art of putting together a manuscript. Earlier in my career, I wrote the papers myself and prepared them for submission. It was a longer process then, since figures

had to be prepared by hand and submissions were made by courier, rather than electronically. With the internet, the preparation and submission processes have changed dramatically, but the basic elements of writing a good scientific paper are the same.

MU: Early on I wrote as if I was writing a story – trying to build to the climax and then stun the reader with how interesting the findings are. Now I try to let them know what to expect right from the beginning, so they can decide if they care enough to keep reading. I start with the figures, write the legends, then the results section follows from that. The discussion and materials & methods grow out of that, and then you know what you need to include in your introduction. At the end you know enough to write a clear abstract, and sum the whole paper up in an explanatory titl4. (Note: When I say "I" write a paper now, I mean that in the sense that I make my trainees do it. Then we go back and forth for revisions.)

JURA: What is your most important piece of advice for students who are writing their first scientific article for publication?

MH: Suggestions for writing your 'first' and subsequent articles: 1. Have your working hypothesis, your approach to test the hypothesis and the key data supporting (or disproving) your hypothesis clearly in your mind. THEN 1. Generate a provisional title that captures the essence of what you've discovered. 3. Line up the figures in the sequence you wish to 'tell the story'. 4. Generate a bare-bones point-form outline of the projected manuscript (just the main headings e.g. Intro/Methods/Results/Discussion with point-form topics that will be included in each section. 5. Write the abstract, according to the instructions for your Journal of Choice. The abstract should concisely 'say it all': what was the main issue/background; what was your new hypothesis; how did you test your hypothesis; what did you find; what are the conclusions/implications of your new data. 6. Go on to write the intro based on your abstract information, including ONLY the background and references relevant to the working hypothesis, and the experimental approach used to test the hypothesis. Many authors currently present their 'main findings' in the introductory section; but that information in the intro. is a 'no-no' for many journals; and it takes away from sucking in the reader to read the entire manuscript. 7. Revise ad nauseam; then run by a colleague or other individual for comments, revise again pending comments; read to eliminate final typos etc; then submit online

WM: As mentioned above, be sure you are writing a compelling, interesting story. Use plain language and be very clear. Ensure that your science is excellent. Importantly, involve all of the co-authors in the preparation of the manuscript. Not only is this ethically the right thing to do, but your co-authors can provide lots of insight that will make your paper better. Finally, don't take rejection personally. You will get rejected from time to time, and you will almost always have to do revisions (I've published over a hundred papers, and have only had one accepted without revisions). Being rejected or having to do revisions doesn't mean you're a bad scientist – it's just part of the business.

MU: Science is very specialized. The vast majority of scientists do not have the time or inclination to read your paper. Your title should be clear enough to let the casual reader skimming through their automated PubMed or Google Scholar search results (you all do this, right?) decide quickly whether or not they care enough to read the abstract. Your abstract should summarize the whole paper – I like to think of it as: if someone was willing to trust you completely, all they would need to read is your abstract. The rest of the paper is there because of course they don't.

6 JURA: How did your 1st first author publication positively impact your scientific career?

MH: My 1st first-authored manuscript contained many of the elements of focus and discovery that underpin the direction my research career has followed since that time: Those elements include: 1. peptide hormone biosynthesis, storage and secretion; 2. peptide-protein isolation and characterization; 3. amino acid analysis, 4. protein-protein interactions; 5. protein physical chemistry, 6. smooth muscle tissue bioassay; 7. peptide hormone structure-activity relationships, 8. receptor molecular pharmacology. Many of these elements can be found in a recent manuscript describing the isolation of receptor/PAR-activating proteinases from cockroach extracts (PMID: 28317204). The overview article that follows provides the background for the impact of my manuscript work on my current career follows. In essence, the skills portrayed in my 1st first-authored manuscript were the essential seeds of what has grown to characterize the work I continue to do today.

WM: My first paper was exciting because it showed that I could do good science that others would read and cite. In a way it was a validation of my chosen career path. I still enjoy the thrill of discovery and sharing my findings with colleagues around the world.

MU: The assay system I developed I then went on to use in a second first-author publication. This work combined gave me a portable NSERC entrance scholarship which let me choose where I wanted to go for grad school – I could also have stayed on at Merck if I had wanted a job.

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University of Calgary Faculty Interviews continued

A unique perspective on one faculty member's path to a successful research career

Derrick Rancourt is a Professor in the Depts. of Oncology, Biochemistry & Molecular Biology and Medical Genetics, University of Calgary. He received his BSc and PhD in Biochemistry from the University of Guelph and Queens University respectively and postdoc'd in the laboratory of Nobel Laureate Dr. Mario Capecchi. He is the Director of the University of Calgary's Centre for Mouse Genomics, which specializes in the generation of transgenic and knockout mice. His research program revolves around the derivation, expansion, differentiation and genetic manipulation of mouse and human pluripotent stem cells, including embryonic stem cells and induced pluripotent stem cells. Over the past several years he has been developing bioprocesses for generating bone and cartilage tissue from stem cells for transplantation. An important feature of the research is the development of methods for expanding and differentiating murine and human pluripotent stem cells in stirred suspension bioreactors.

Like many, I started in University with the intention of going into Medical School. However, I soon became enamored by the theory of evolution, having not been introduced to it in high school. In my second year, I was inspired by the work of Brinster and Palmiter, who made the first transgenic mouse, demonstrating that forced overexpression of the human growth hormone resulted in animals that were twice the size of their littermates. Seeing opportunities in this brand new field, I made it my mission to become a genetic engineer. After a mind-numbing experience working at a steel plant during the summer after my first year, I decided that the only way I was going to become a genetic engineer is if I procured relevant research experience.

It's funny how we bumble along towards our career goal. Having read Stephen Shapin's *The Scientific Life*, I now know the importance of experimental research, but at the time my instincts told me that research experience would pave my way. People say we are products of our environment and my path to becoming a genetic engineer was a circuitous one. This is largely because in Canada molecular biology, let alone genetic engineering, was in its infancy. At the University of Guelph, there was only one early adopter of molecular biology and getting into his lab seemed next to impossible. Knowing what I know now, I should have engaged him directly and asked him to help me with my plan. But I was gutless at the time. I did not know the importance of network problem solving and how it offered the potential of getting me to my goal faster. Instead I chose the path of least resistance, working for one of his colleagues who had taught me genetics.

I liken my research lab experience to that of the budding artists who worked in the Bottegas of Renaissance Florence. Here, entry level trainees did all the "joe jobs", they cleaned the chicken coups and

collected the eggs used to make the paint for those higher up on the food chain. Similar to cleaning chicken coups, my first lab experience was to prepare "fecalase", an enzyme extract from my own feces. Part of the Ames mutagenicity assay, the theory behind fecalase was that it simulated the conversion of pro-mutagens in the gut. In my project, I used the Ames test to investigate the mutagen content of tannin pigments found in red wine.

Although it wasn't genetic engineering or molecular biology, the project gave me exposure to genetics research and oenology (who knew wine-making/-tasting was a science!). This research experience provided me with an important career entrée. Much like the Florentine Bottega, I was keen to pay my dues as a novice and boy did I pay. I'll never forget how my former boss would snicker whenever it was time to prepare a fresh batch of fecalase. Just to rub it in, he would hand me a box of oatmeal cookies a couple of days beforehand, advising me that enzyme activity would be enhanced if I ate them a day or two before the prep.

Jokes aside, my first academic mentor helped introduce me to academia. He helped me to secure a spot in that molecular biology lab and to get my first genetic engineering position. It was through his kindness and my sacrifice that I am here today.