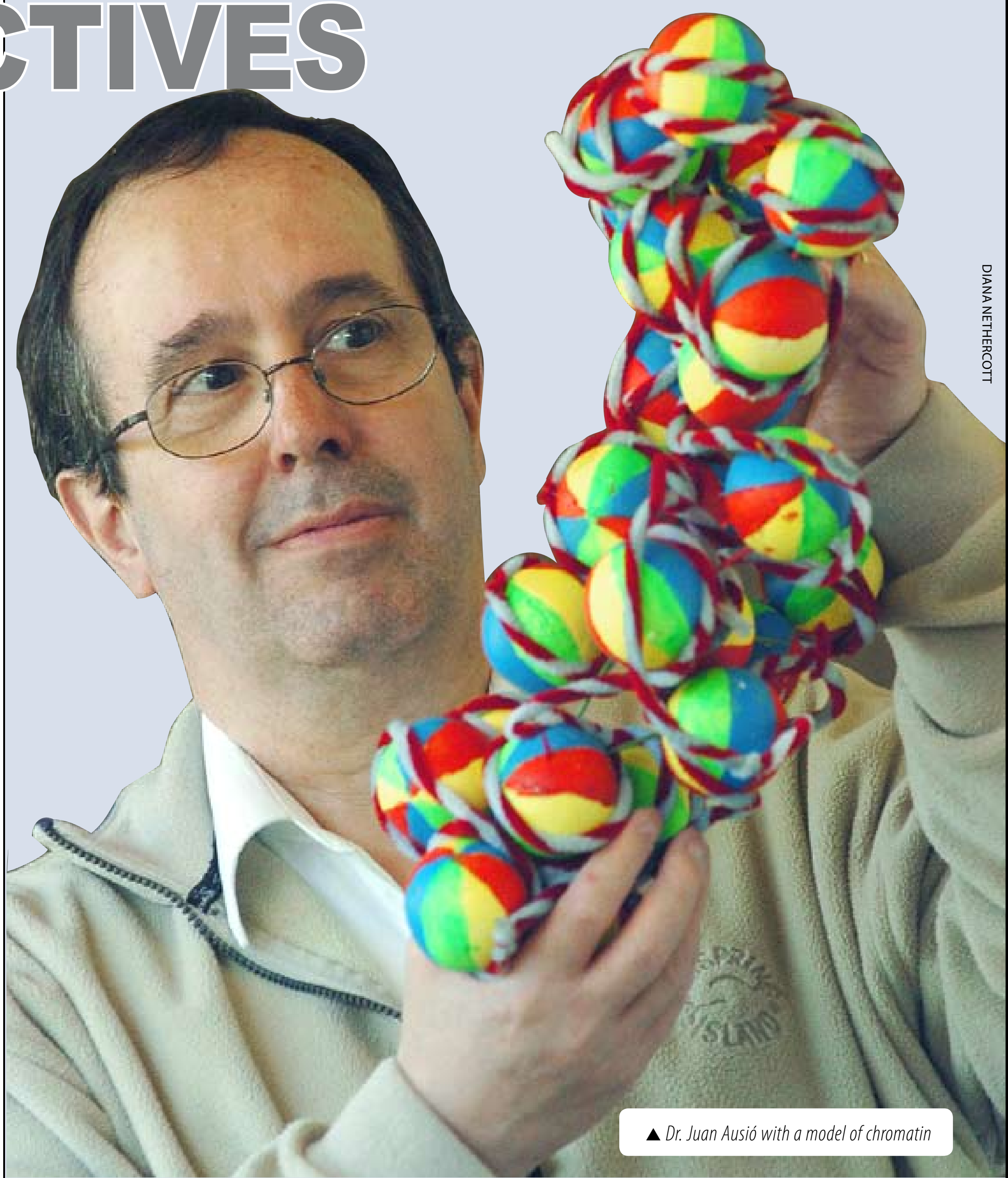
UVic knowlEDGE

DNA DETECTIVES

A genetic structure you've probably never heard of is the key to new disease treatments



▲ *Dr. Juan Ausió with a model of chromatin*

DIANA NETHERCOTT

Most of us are familiar with DNA, genes and proteins and how they work together to determine who we are, how well our bodies function, and what diseases we're susceptible to in our lifetimes.

And then there's chromatin.

Say what?

Oddly enough, chromatin is just as essential to our existence, yet few of us have ever heard of it, let alone know what it does. Dr. Juan Ausió is working hard to change that. The University of Victoria biochemist studies how strands of DNA and the special proteins associated with them—collectively known as chromatin—interact with one another in healthy and damaged cells.

What he and researchers in his lab are finding out will help us treat diseases such as breast and prostate cancer and genetic disorders such as Rett Syndrome.

"How DNA is packaged in our cells is one of the miracles of life," says Ausió. "Laid flat, the DNA in just one of our cells would be two metres long, yet it manages to fit into a cell nucleus that measures a fraction of a millionth of a metre."

To accomplish this Houdini-like feat, portions of each DNA molecule are wrapped around proteins known as histones. This wrapping causes the DNA to twist around itself, forming tight coils. DNA spends most of its time in this coiled state—known as chromatin.

But the DNA has a job to do, and chromatin plays a big role here, too. Chemical signals within the cell tell the chromatin to either unfold or to wrap more tightly around itself. "Exposed genes are switched on, their DNA is read and the corresponding protein is synthesized and sent out to do its work," says Ausió. "Genes that are in tightly folded regions of chromatin can't be expressed."

Understanding the structure of chromatin, its pivotal role in gene expression, and what can go wrong and why, is the theme of several projects in Ausió's 12-person lab.

With the help of research assistant Allison Maffey, Ausió is investigating what chemical miscues take place with chromatin that ultimately lead to prostate cancer. PhD student Diana Dryhurst is looking at the role of chromatin when cancer cells develop a resistance to tamoxifen, a breast cancer drug.

And PhD student Anita Thambirajah is studying a protein known as MeCP2, which directly affects chromatin structure. A mutation to this protein causes Rett Syndrome, a degenerative neurological disorder that affects roughly one in 10,000 girls.

"This is a classic example of a chromatin-related disease," says Ausió. "Most intriguing is that this mutated protein is found in all body cells, yet only brain cells are affected. We still don't know why."

The ultimate goal of all the research in Ausió's lab is to help develop new drug and treatment therapies. "If we can fully understand what chemical signals cause chromatin to change its structure, activating or hiding certain genes," he says, "then we can work on ways to fix the mistakes that cause disease."

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The DNA component of chromatin stores biological information in units called genes. Human DNA consists of approximately 30,000 genes.

The cells of all higher organisms—including fungi, plants and animals—use chromatin to "package" DNA to fit inside their nuclei. Simple organisms, such as bacteria, don't need chromatin because their small genomes have ample room inside their cells.

Juan Ausió has been studying the mechanics of chromatin since 1974. Graduate students in his lab are currently collaborating with researchers at Victoria General Hospital, the Prostate Centre at Vancouver General Hospital, and the BC Cancer Agency's Vancouver Island Centre.

Ausió's work is funded by the Canada Foundation for Innovation, the B.C. Knowledge Development Fund, the Canadian Institutes for Health Research, and Science and Engineering Research Canada.

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In 2004-05 University of Victoria graduate students were awarded a total of $3 million in research grants from the three federal granting councils, up 25 per cent from the previous year. Their success rate in attracting research grants is consistently above the national average.