Dr Bazan has featured in so many magazine articles, from Forbes to his local New Orleans Living, that his background and upbringing is almost a matter of public knowledge. Born in Los Sarmientos, Tucuman province, Argentina, it was in Tucuman City that he studied medicine. Drawn to this subject after experiencing first-hand the chilling effects of neurological disease in his family, he completed his training at Harvard Medical School after a year’s stint in New York’s Columbia University College of Physicians and Surgeons.

Those who witnessed him achieve selection to the faculty of the University of Toronto at the age of twenty-six must have known he was destined for great things. From here he moved back to his home country of Argentina where he became the founder of the Instituto de Investigaciones Biogúcitas. He also set up a graduate programme in biochemistry and assembled a large group of students and fellows to work in his newly established lab. With exceedingly limited equipment and resources, he struck on two budgetarily feasible ideas: using early amphibian (toad) development as a model of cellular membrane biogenesis and using the retina to study the brain – a decision that would prove enormously beneficial to his work. This productive period was, however, cut short in the early 80s by the political turbulence in the country. In fear of his safety, Dr Bazan was forced to leave his successful institute and flee with his family back to the United States.

The move to LSU quickly followed, where a few years later he was asked to become the founding Director of the Neuroscience Center of Excellence. There he certainly found his scientific home, but it is as likely also that his long stay is due to the finding of a different satisfaction in the cultural melting pot of New Orleans. He credits his faith and family, along with the strong relationships he has built with many around him, as the grounding force that has helped him overcome the hurdle of sudden displacement and other setbacks, among them his triumphal bout against advanced inoperable cancer 14 years ago. Dr Bazan celebrates rather than laments the difficulties he has faced, saying ‘adversities bring strength and renewed perspective’.

His awards, honours and collaborations make for a very long list, so long that no one seems to have the time or space to publish it in full. From membership of editorial boards across Europe and the American continent, to chairs, elected to Academic Societies and fellowships of distinguished faculties in the United States (US) and further afield, Dr Nicolas Bazan is a name synonymous with first-class neuroscience research. As Michael Moskowitz, Professor of Neurology at Harvard Medical School/Massachusetts General Hospital puts it, he ‘is passionate about everything he does in life, especially his science, and this passion has driven a lifetime of discoveries that have inspired both his students and colleagues’.

THE MAN OF SCIENCE
Dr Bazan focuses his attention not on the lucrative or straightforward cases, but on those neurodegenerative diseases for which there is no known cure. It is perhaps even more telling therefore, that he has made such inroads into the understanding of the underlying pathology. Considering the difficulty of establishing treatments for such diseases, it is no wonder that Dr Bazan himself believes that ‘the only way to conquer them is by getting a new understanding of the cellular and molecular mechanisms engaged in the onset and early progression of brain and retina diseases’. This has been his focus during a lifetime of research, a labour which he says he has been, ‘lucky to have been able to contribute to’.

Here again the list just goes on and on. There have been breakthroughs and in the understanding of the response to the foremost causes of long-term disability in the US – cerebral ischaemia (stroke) and seizures (as in epilepsy) – the mechanism of which is now known as the Bazan Effect (as discovered that Acyl DHA which is now known as the Bazan Effect (as found for a very long list, so long that no one seems to have the time or space to publish it in full. From membership of editorial boards across Europe and the American continent, to chairs, elected to Academic Societies and fellowships of distinguished faculties in the United States (US) and further afield, Dr Nicolas Bazan is a name synonymous with first-class neuroscience research. As Michael Moskowitz, Professor of Neurology at Harvard Medical School/Massachusetts General Hospital puts it, he ‘is passionate about everything he does in life, especially his science, and this passion has driven a lifetime of discoveries that have inspired both his students and colleagues’.

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Bengt Samuelsson, a Swedish researcher and Nobel Laureate at the Karolinska Institute in Stockholm, defines it, ‘the Bazan effect is the release of polyunsaturated fatty acids during seizures and ischemia’. There is the identification of targets for novel therapeutics, and the uncovering of the novel compounds themselves, to combat the onset and progression of epilepsy, a condition which 30% of US patients do not have adequate control over. Or you can point to the identification of a novel protective molecule to hopefully slow the onset of Alzheimer’s disease. Dr Bazan has also targeted chronic pain by developing a novel generation of non-addictive, non-toxic analgesics, which is bringing to market via a new start-up company he co-founded specifically for this purpose, using the findings from his work on injury and inflammation of the brain.

His work has been recognised by distinguished colleagues around the world. Dr George Carman, Chief Scientific Officer at the New Jersey Institute for Food, Nutrition, & Health, Rutgers University, says Dr Bazan ‘has dedicated his career to conducting the highest level of science to the underpinnings of brain function and diseases’. His work has also included a related and equally challenging area, blindness caused by retinal degeneration, and once again he is bringing his experience and intellect to bear with stunning effect.

A MAN CAN BE KNOWN BY HIS EYES

The focus of Dr Bazan’s work from its discovery at the earliest stage in his career is the brain release of arachidonic acid and docosahexaenoic acid (DHA) upon stimulation. DHA is an omega-3 fatty acid, the precursor of which is only available from dietary sources, and is retained in higher levels in the brain and retina than any other body tissue. DHA is a key component of membranes engaged in brain and retinal function, acting at the junction between brain cells known as the synapse, and in retina photoreceptors. This molecule has been the subject of intense study by Dr Bazan and his colleagues.

The systems employed by the team have been many and varied, but it was during their use of the retina (the light-sensing part of the eye directly linked to the brain) as a model for research on neurons that DHA’s role, particularly that of bioactive derivatives, in retinal function and disease was established. Using this approach, they uncovered the mechanism by which DHA is accumulated in the differentiated neurons, the photoreceptor cells, having been absorbed from the diet. Dr Bazan postulated and then demonstrated both the ‘long loop’ of transport from the liver to the brain and retina, as well as a ‘short loop’ by which this fatty acid is recovered back to replenish the cells of the retina. This process assured the Bazan team of DHA’s status as a key molecule in normal neural function.

They then went on to further elucidate the fate of this molecule as it is first cleaved and then modified by a range of enzymes to produce bioactive docosanoids, molecules which are now known to promote homeostasis and neurorestoration (maintenance and repair respectively). One such of these was named Neuruprotectin D1 (NPD1) because of its role in fostering homeostasis, inhibiting uncompensated inflammatory signals and preventing apoptosis (programmed cell death) as well as other forms of cell death. The discovery that the availability of this potent molecule is decreased, along with its precursor DHA, and the enzyme that makes one from the other, in the brain memory areas from early stage Alzheimer’s Disease (AD) patients in particular, convinced Dr Bazan and his colleagues that its presence is likely essential in preventing the onset of neurodegeneration. As the retina photoreceptors which provide the stimulus for sight are a type of differentiated neuron, it seems logical that a substance that prevents the death of neurons in AD could also be involved in age-related macular degeneration (AMD), the loss of sight associated with retinal cell death, as well as other inherited retina degenerations.

Dr Bazan has led the way in describing the complex interplay of molecules involved in the management of homeostasis in retinal cells, particularly the retinal pigment epithelium (RPE) which is the layer of cells nourishing and sustaining the retinal visual cells. His work is so important it has been described by Prof Joan Miller, Professor and Chair of Ophthalmology at Harvard Medical School, as ‘a lasting contribution to our understanding of the role of lipids in the retina, especially their function as modulators of neuroinflammation, which is the basis of so many ocular diseases’.

THE RENAISSANCE MAN

Dr Bazan’s most recent research is just the latest in a lifetime of discovery. Bengt Samuelsson describes him as, ‘a leading neuroscientist and eye researcher’ and points to his work on the Bazan effect, showing that his influence is truly international. However, all his colleagues attest to knowing someone whose intellect is not constrained to a single subject, who has made as much of a mark in the other aspects of his varied life as he has in the scientific community. Prof Edmond Fischer, Nobel Laureate and Professor Emeritus of Biochemistry at the University of Washington says, ‘What impresses me most about Nicolas is his enduring enthusiasm and passion, not only for science, but for all of the wonderful things life has to offer. He is the epitome of the renaissance scholar.’

Harnessing the power of the arts

Dr Bazan has, in addition to his successful scientific career, embraced the arts with equal success. His two published novels (and there are more waiting for publication) follow the life of a neuroscientist. One of these, Lita Vida: A Fable of Music and the Mind, has been made into a compelling and poignant movie Off Mind and Music – a process that Dr Bazan was involved in throughout.

The film traces the encounter between a successful neuroscientist and a captivating street musician with Alzheimer’s disease. For Dr Bazan, the act of taking his deep knowledge of the world of neuroscience and translating that into a thought-provoking narrative has created a very powerful tool: ‘I wanted to contribute to removing the stigma of mental illness in society, because mental illness of any kind is just a disease. I wanted also to create awareness about Alzheimer’s disease, and in a way convey a message of hope that science may actually conquer this disease one day.’

‘In art it’s the same,’ says Dr Bazan, ‘because one can, in an oil painting, illustrate the beautiful, and yet sad, chaos that happens in the brain during Alzheimer’s disease. His dialogue with brilliant artist Taryn Möller Nicoll during her residency at LSU Neuroscience Center of Excellence has led her to create a visually arresting portrait of the degenerative processes that occur in the brain.

With the tools of writing and art up his sleeve, Dr Bazan is lifting the unseen neurodegeneration that underlies so many conditions into the light.
What first piqued your interest in neuroscience?

Well, it was a very early childhood experience that I had. I was six or seven years old, and an aunt was taking me to a piano lesson. To make a long story short, she had an epileptic seizure on the street. It was a very traumatic experience to me – all the pianos flew into the air due to a grand mal seizure. My mother told me that my aunt, her sister, had epilepsy which was a brain disease, and that stuck in my mind. It was not something that I always thought about but very likely, on reflection, that motivated me to go to medical school and to become interested in the brain and neuroscience.

Farther on, my mother strongly encouraged me towards medicine. She really stimulated me to read and to think about medicine, and her message was that by doing something in the medical field I could help people with diseases that were very difficult to cure or to treat.

And a lot of your work relates to neurodegenerative diseases. How did you become interested in them?

Well, it started with epilepsy. During my time at Harvard Medical School I was a fellow at the Massachusetts Mental Health Centre. This was a psychiatric hospital with a major research effort. I was very impressed by a therapy that was being used at that time. I was six or seven years old, and an aunt was taking me to a piano lesson. To make a long story short, she had an epileptic seizure on the street. It was a very traumatic experience to me – all the pianos flew into the air due to a grand mal seizure. My mother told me that my aunt, her sister, had epilepsy which was a brain disease, and that stuck in my mind. It was not something that I always thought about but very likely, on reflection, that motivated me to go to medical school and to become interested in the brain and neuroscience.

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That's really interesting, isn't it? It certainly suggests an area to look into. Well those things give us hints in order to go and design experiments where we can actually go into the intimacy of the molecular principles that are involved in the development of diseases like these. Many laboratories now are using stem cells-like approach as well. In my laboratory, we are reprogramming adult cells into induced pluripotent stem cells (iPSCs) that become neurons, enabling us to get an insight into molecular principles of neuronal survival and neurodegeneration. Then, having those cells in the laboratory, one can identify which are the molecular mechanisms that are actually changing, and also one can use these cells to test experimental compounds that could become drugs or treatments in the future. So the development of neurons differentiated from patient-specific iPSCs can recapitulate molecular phenotypes of Alzheimer’s disease or other neurodegenerative diseases. This human genomics approach will also facilitate implementation of precision medicine.

To go back to your question, “When can we have a treatment?” the answer is, there are enough tools and information that make us very optimistic that we are going to see at least effective treatments to slow down onset and early disease progression in the not too distant future.

Which is fantastic news, isn’t it? It's amazing that things are progressing like that. As a global population we are getting a lot older. Do you feel that ageing and age-related diseases are getting enough priority and focus at the moment? I believe so. I want to take this opportunity to tell you that ageing is not a disease. Many people will age successfully, particularly when one of the conditions that can lead to a deficit of liver enzymes for DHA is regulated because the retinal pigment epithelial cell is the most active phagocytosis in our body. We have many, many cells in the body that do phagocytosis and the function of these molecules is to remove the dead cells, eliminating debris, eliminating foreign bodies but those RPE cells eat the tip of the photoreceptor by phagocytosis in order to renew that structure. That photoreceptor cell is obviously essential for vision. DHA. So we identified those processes, and certain molecules back to the retina to rebuild them. This is a fascinating process. Yes, it is fascinating. It’s called phagocytosis and every day, the tip of each photoreceptor is shed and is phagocytosed by this cell. The RPE cell then processes the remains of the photoreceptor and retrieves certain molecules back to the retina to rebuild part of the photoreceptor cell daily. This is called renewal of the photoreceptors and among those molecules that are retrieved is DHA. So we identified those processes and named the loop that brings DHA back from the cell to the retina, the short loop (the one that brings DHA from the diet, truly from the liver, to the retina and brain, we named the long loop several years ago) and we’ve been trying to understand how this process is regulated because the retinal pigment epithelial cell is the most active phagocytosis in our body. We have many, many cells in the body that do phagocytosis and the function of these functions use very important cells. When you first started looking at the relationship between DNA and the retina you were using the eyes as a way to find out more about the brain, and then you started uncovering a lot of really interesting things about the eye itself. Is that right? Absolutely. This was Argentina in the early 70s and we didn’t have many resources. We would go at three in the morning to the slaughterhouse, get cows’ eyes as they processed the meat, bring them to the laboratory and peel the retina off. And that was a beautiful nature-made brain slice. We began by asking questions that we were interested in because of the neurological and ophthalmological implications. And suddenly it became very apparent that diseases of the retina, like age-related neurodegenerative diseases, for example Alzheimer’s, and other diseases of the brain have mechanisms in common. The retina is an exceptional model to ask questions of the brain, but it’s also a very important organ that fails in ageing and many vision-related diseases, some inherited, some age-related. One aspect that fascinated me very early on about the retina, was the cell called the retinal pigment epithelial (RPE) cell which can eat the tip of the photoreceptors every day in our eyes. This necessity, due to lack of funding in the early 70s, made us design experiments using toads that became ideal to ask these retina questions.

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It’s very inspiring to hear about everything that are achieving and have achieved. Are there any things that you’re particularly proud of? We’ve been very proud and I’m very proud of them. Each of them has their own successes and their own activities, and so that’s something that I’m very proud of. And now they have given us 12 grandchildren and two additional step grandchildren. Of course, my wife, also a scientist, has been fundamental to everything that we have talked about today. And I’m very proud to have a lot of colleagues in different stages of their scientific life working with me. So, those are very important components of my life.

RESEARCH OBJECTIVES
Dr Bazan’s work focuses on uncovering the brain processes that underpin neurodegenerative diseases such as Alzheimer’s and Parkinson’s, age-related macular degeneration, traumatic brain injury, pain, epilepsy and stroke. Much of his current work centres on deciphering the molecular principles of mitochondrial significance in cell survival, autophagy, neuroinflammation and single cell transcriptomics that underlie neuroprotective and neurorestorative activities of DHA and its derivatives, including novel approaches to neural stem cell generation and applications.

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COLLABORATORS
Nicos Petasis (USC, CA); Julio Alvarez Bulla Gomila (U. Alcala, Spain); Dennis R Rice (Novartis, Cambridge, MA); Professor Gerhard Lents, Ludmila Belayev and Walter Lukiw (LSU, New Orleans); Ricardo Palacios Pelaya (Chater Lab, Spain); Andy Obenaus (LLU, CA); Marianne Schulzberg (KI, Sweden); Charles N Serhan (Harvard, MA)

BIO
Dr Bazan is the founding Director of the Neuroscience Center of Excellence at the Louisiana State University Health Sciences Center, School of Medicine, New Orleans. He has been appointed to the highest academic rank in the LSU System; a Boyd Professor (1994-present) and is also the inaugural founder of The Ernest C. and Yveta C. Villeray Chair for Research in Retinal Degeneration (2006-present). Foreign Adjunct Professor of Neuroscience in the Department of Neurobiology, Cancer Sciences and Society, Karolinska Institute, Sweden (2016-); Chairman Emeritus of the Board of Governors of the Association for Research in Vision and Ophthalmology (ARVO) Foundation.