**Is there more to life than genes?**

**St Andrew's James Gregory lecture Oct 2010**

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**1. Quotation from Paul -** 1 Corinthians 12:13

***Slide 3 St. Paul***

The body is a unit, though it is made up of many parts; and though all its parts are many, they form one body. If the foot should say, "Because I am not a hand, I do not belong to the body," it would not for that reason cease to be part of the body. And if the ear should say, "Because I am not an eye, I do not belong to the body," it would not for that reason cease to be part of the body. If the whole body were an eye, where would the sense of hearing be? If the whole body were an ear, where would the sense of smell be? The eye cannot say to the hand, "I don't need you!" And the head cannot say to the feet, "I don't need you!" On the contrary, those parts of the body that seem to be weaker are also indispensable.

St. Paul is referring to parts of the body that you can see, but equally important are the millions of molecular machines and processes that we cannot see but nevertheless sustain our every waking moment. These are no less a part of the body and it makes no sense for the neurons say to the heart I don't need you, neither can proteins say to the sugars or lipids, I don't need you, nor can the genes to say to the proteins,, I don't need you.

And so, continues St. Paul, we should make no division in the body, but its parts should have equal concern for each other. If one part suffers, every part suffers with it; if one part is honoured, every part rejoices with it.

The body is a highly complex entity which is constructed in such a way that it can interact effectively with the environment on which our survival depends. We are part of a holistic system – the body cannot say to the atmosphere, I don't need you, and live; we cannot say to other people and other species, I don't need you and continue to live.

***Slide 4 Organisms***

If we wish to describe a human being or any other organism, it is hard to know where to begin because there is no single beginning. We might try to begin chronologically, but everything, including the fertilisation of the egg by a sperm, takes place in an environment that was prepared before the event. We might try to begin with an atom or the smallest component of a cell but very quickly there would be so many options that a linear story would shortly become impossible. The organisation of a human being, or any other creature, does not have a single, simple hierarchy. There is no means of describing ourselves in a linear fashion for there are countless starting points and hundreds of feedback loops that pass information around the body. This allows us to respond to our constantly changing environment and to engage in the co-operative behaviour that enables us to survive in a challenging world.

***Slide 5 Genes***

However, in our search to discover ourselves, our genes are a good place to start for they make each of us unique. They do not act unilaterally, they do not constitute a blueprint for our bodies; however but they do contain information that represents potential and imposes constraints.

***Slide 6 genes***

We each have our own particular version of the human genome inside our cells. From our 30,000 or so genes, the systems they operate and the environment that surrounds us within and without, we derive purpose, assume agency, transcend the limitations of our environment and accept constraints that we cannot change. To this extent our genes are indeed us; these we can claim are peculiarly our own.

**So what are genes?**

They are one of the 3 biological alphabets that provide the building blocks of the natural world. They are attached to strands of DNA which is very tightly folded into 23 chromosomes in humans, some of which are bigger than others. They are

numbered roughly in order of size. There is enough DNA in the human body to stretch to the sun and back 600 times!

***Slide 7 list 1***

The way in which geneticists describe genes is changing.

1. Genes were once defined as units of inheritance. Since then they have come a long way.

2. A more recent definition is that genes are DNA based units that can exert their effects on the organism in which it is located through RNA or protein products.

3. Genes are one of 3 biological alphabets. They are composed of combinations of 4 bases (Adenine, Thymine, Guanine and Cytosine) and are assembled on very long linear molecules of deoxyribonucleic acid. One strand of DNA with the 4 bases attached and its complementary partner combine to form the famous double helical structure.

4. Genes are arranged on 23 pairs of chromosomes in humans (A chromosome pair is one pair of DNA molecules)

***Slide 8 list 2***

5. Genes can replicate themselves. Also the DNA can be specifically unravelled to expose particular genes when they are needed to make proteins. The genes are copied to make messenger RNA which finds its way to the ribosomes located in a part of the cell called the Endoplasmic Reticulum. In the ribosome mRNA is edited and translated into proteins. These are linear molecules composed of amino acids linked together. 3 bases code for one amino acid. Human beings make 21 different amino acids. The gene is ‘read’ from one end to the other and amino acids are linked together in the order specified by the base triplets to form the protein.

6. Genes can be altered, that is mutated, when the order of the bases is changed. Mutations alter protein sequence and structure which may not alter the function of the protein, might lead to new opportunities or sometimes to disease.

***Slide 9 list 3***

7. Many genes code for proteins which have multiple functions - all cells contain all of them but genes are only expressed in specific temporal and spatial locations. They are carefully controlled switches that allow the growth, repair and differentiation of the body.

8. Very few genes give rise to a single consequence or even act alone. For example, 100 genes are related to height, and of course nutrition also plays a role – determining height is a very complex process and no wonder that we cannot add one cubit to our stature by worrying about it!

9. Genes respond to signals from their environment telling them that the protein they have the code for is needed. They are devices for extracting information from the environment.

10. To a large extent genes have the potential to determine the organisation of their own body within an awe inspiring complexity. Just as music has an existence of its own but requires an instrument to be realised, genes need a body in which to be expressed. However a person may have the genetic background to be a great violinist but if they are never given an instrument or do not practise, their gift will never be developed. Some things are less about genes and more about opportunity.

***Slide 10 EGFR***

11. Genes have interchangeable parts that code for important functions. During evolution when a protein had a useful function the key parts of it were retained– that is why we have large numbers of genes in common with fruit flies, the roundish flat worm and the stickleback. *Epidermal growth factor, which has a crucial role in cell growth and proliferation, is present in hundreds of species from lampreys to chimpanzees. * The gene may mutate a little and

the * protein sequence will change but if that change is so great that it means the protein cannot function adequately then the mutation will be lethal and will not persist in the species.

***Slide 11 EGFR***

You can see in this slide the amino acids in one domain are crucially important for the function of EGFR. Almost of the amino acids in this region are the identical in every species.

***Slide 12 Biological alphabet of genes/proteins***

Powerful though they are, genes only represent potential, and of themselves they can do very little, just as an eye disconnected from a brain has limited function. They are simply linear molecules made up of 4 functional groups - the bases. Genes are packed tightly into chromosomes and there they would stay if it were not for proteins called transcription factors that open up sections of the DNA and start the process that leads to the production of proteins. mRNA is copied from the DNA and eventually the ribosome locks around RNA to begin making the proteins. The ribosome is a huge, very complex molecular machine that is made up of 4 RNA molecules and 80 different proteins. The ribosome links together a series of amino acids, one of which has been collected by each triplet of bases (codons) on the transfer molecules. These amino acid chains are folded into the proteins, and these are the operational units that, in contrast to genes, actually do many things. The process is unbelievably efficient – for example 100 trillion molecules of haemoglobin are produced in our bone marrow every second.

***Slide 13 Proteins***

We can now move up to another level of complexity as function emerges from a protein; the fully folded epidermal growth factor receptor has been made and transported to the cell surface. Now we can understand a bigger picture: EGRF controls cell growth and proliferation. When it binds to a molecule in the serum (EGF) it sends signals to the nucleus of the cell that result in the genes expressing the proteins needed for cells to grow. We are especially interested in EGRF because

it is often over expressed on cancer cells allowing uncontrolled growth and it a drug target.

***Slide 14 Biological alphabets Glycosylation***

But this is not quite the end of the story - after synthesis as a linear chain many proteins, including EGRF, that are destined for secretion or for the cell surface enter what is known as the secretory pathway in the ER where they undergo folding and also acquire various modifications, especially sugars which is my particular area of expertise.

***Slide 15 Glycobiology Talk to slide***

Here you can see a diagram showing the different parts of a cell, a secreted gp epo and the surface of a cell where the sugars attached to the cell surface proteins are stained black.

***Slide 16 CDG***

Genes can be altered (mutated). This happens for example, when one base changes, perhaps because of miscopying. This in turn changes the sequence of amino acids and thus alters protein structure. This may do nothing but if it is a sensitive part of the protein it can have a dramatic effect. It might give the protein an alternative useful function but more often it builds an inactive protein that can cause serious disease – like CDGs where the mutation in a single critical gene, *Mgat 2*, that makes an enzyme involved in sugar processing, leads to a heavily compromised individual. You can see how unlike a healthy person's profile the sugar pattern of this patient is.

***Slide 17 Blood group antigens***

Blood group antigens are also sugars and are genetically determined. Apart from causing major problems for blood transfusions, these tiny differences in the sugars can make some people (blood group O) more susceptible to pathogens such as noro virus and cholera.

***Slide 18 Sickle cell anaemia***

Sickle cell trait occurs because of a coding change in the DNA for haemoglobin, a substance in the blood that transports oxygen. Mutated haemoglobin results in structural defects of red blood cells, which severely compromises oxygen uptake and leads to anaemia. In Africa, there is a high frequency of this mutation, where cases of malaria are high. Those who carry the sickle cell trait have anaemia, however they avoid malaria since the parasite cannot replicate in sickle cells.

Another genetic variation, this time of the HLA-B gene, HLA-B53, which some people carry make a particular immune molecule which protects them against severe malaria.

So the sequences of our personal genomes can give us protection against some pathogens but be risk factors for others.

***Slide 19 Darwin's finches***

Genetic diversity not only makes each of us unique, it also helps to ensure the survival of our species. Darwin's finches on the Galapagos Islands have been studied for many years. There are several subspecies with different kinds of beaks that are specialised for different types of food. Some birds do better in dry seasons, some in the wet. Whatever the conditions one or other subspecies will be adapted to survive.

**Our** individual genetic differences have enabled us to withstand plagues, and also to specialise and divide our tasks within a community, liberating time for creativity and imagination - we could never have progressed if we could not share skills. Economies arose because of exchange of objects and agreements to specialise. Our culture did not shape us as a species, it developed because of our collective abilities and because of our development of language and technologies and our expanding brains.

***Slide 20 Brain***

Our brain is the most complicated organ we have, and we only just beginning to understand its genetics, its proteins and sugars and how it works. We do know that many of our activities are not normally exercised under conscious control. The brain is smart – there are about 40 firings/sec at the conscious level compared with 40 million at the subconscious level. This allows the brain to give maximum attention to things which need conscious, intelligent, executive decisions.

The brain is plastic and continues to develop and adapt from 3 weeks after conception to the end of our lives. It responds to experience, forming new pathways and, for example, the prefrontal cortex is not fully developed until about the age of 25.

***Slide 21 dealing with complexity Isabella Talk to slide***

We have outlined a path that takes us from genes to the most complex organ on the planet, the human brain. We have seen that the cell can take messages from its environment, transcribe genes to proteins to produce fully functional molecules. At each step we can see that small components such as bases, give rise to entities that are more complex and diverse (the genes, the proteins), and that these complex and diverse entities can themselves be viewed as simple and unified when we analyse what is happening the next level of complexity (the cells, the tissues, the organs) and eventually the whole person).

Describe slide.

**But the big question is: Who or what is ultimately in control ?**

One thing we have learned in recent decades, is that life is infinitely more intricate than we imagined. New technologies have enabled us to open up the field of biology to explore the chemistry that underpins it. We can now appreciate that we are made up of thousands of dynamic systems, many completely outside our conscious control. It seems that there is nothing ultimately in control, no single thing directing and micro-managing us. Each small part faithfully carries out its role, unaware of the place it has in the big picture until finally we reach the level of consciousness. Even

then it seems that this is a co-operative integrated process with many inputs for inside and outside of our bodies.

**So what initiates action?**

It used to be axiomatic that reductionism was the scientific method that would allow us to describe and control everything, and indeed it is still an essential part of scientific investigation. But it is not enough; in modern biology we have reached the limits of our ability to rebuild the whole picture from its parts. As we begin to appreciate the level of detail that underlies the most simple operations in our bodies we need all the power of modern bioinformatics to work out how to assemble large amounts of non-linear information.

***Slide 22 Escher***

Trying to deal with complexity and emerging properties is a major challenge that defies a simplistic view of the world. Many things do not fall neatly into boxes and we are currently trying to understand the tipping points that lead to committed action such as the differentiation of a stem cell. We need to come to terms with the reality that everything is dynamic, many entities have several options when it comes to activity and we need to visualise thousands of interactive pathways, preferably simultaneously.

***Slide 23 Schematic***

I believe I have said enough to convince you that at the biochemical level we are certainly more than our genes. Genetic determinism is not a general feature of our individual genomes for the external and internal environments are the backdrop that triggers gene expression. Our inner worlds matter too, for our brains have given us the possibility of imagining what we cannot see and have not experienced. It is remarkable that our material brains can engage with abstract ideas that come from other people and emotions that are non-material and then take action. As many sages and ordinary people have testified it is also entirely possible for us to experience insights that did not arise from rational conscious deduction, and at the time, were beyond description.

***Describe current slide***

***Slide 24 penguins***

The challenge now is to discover how we can relate all the detailed information we have about our physical bodies to the deepest yearnings and insights of the human spirit. Science is an incredibly effective way of understanding the world but alone it is not enough. An intellectual understanding of causes and dealing with the consequences are not the same thing.

***Slide 25 Thinking man***

Science may provide a rationale for the basis of our ethics, our relationships with others and our deepest experiences of love, joy, beauty and hope. But understanding how we work is not the same thing as understanding how we should live. Science, like Nature, is ethically neutral; we have to think out the rest for ourselves.

To be more specific, if we reject predestination imposed by absolute genetic determinism and if we no longer subscribe to the concept of a god who controls our lives through divine intervention, then we ourselves become responsible for determining the purpose of our lives, and that means taking into account the consequences of our personal genomes, those of others and our environment.
Even if it did turn out that we are genetically predetermined or controlled like puppets by some god out there it would not really help because few of us really believe that we have no personal freedom or responsibility. Our perception of ourselves as having some level of self determination and agency might just be an illusion I suppose, but the alternative, that we have neither of these, would seem to fly in the face of common sense.

***Slide 26 Nebula***

In any case, this is in fact how we live, for regardless of our certain knowledge that our lives are finite, that the earth will eventually be subsumed and in the end all that we know will no longer exist, we continue to imbue our existence with meaning. This demanding approach to life, which in the long term appears to be rather irrational

seems to need addressing. To approach this question, I believe we need more than a mechanistic view of our world, indispensable though that is.

***Slide 27 Books***

If we are to make the complex choices that confront us with sound judgment then we need to complement the magnificence of our modern scientific insights with experience from other windows on the world. These include art, music, literature and the great philosophies and religions of the world.

***Slide 28 Zeldin***

The scientific enterprise itself is enabled when imagination and insight are combined with rational thinking. Bringing ideas from our unconscious 'knowing' to the conscious mind where they can be evaluated and codified is a practice that every scientist, artist, mathematician and philosopher will recognise. Scientists use model systems and equations to express ideas which begin in the imagination. Religious thinkers use poetry, ritual, symbol and myth to express theirs. Scientists test their models in experiments. Religious leaders and philosophers develop internally consistent doctrines and dogmas. Those who follow a spiritual path test their inner experience in their own lives.

***Slide 29 Buddhist flags***

For millennia people have projected their profound internal awareness onto higher beings of all kinds in attempts to link the sacred with the secular. Many reasons have been rehearsed by anthropologists for this practice. However, God in essence is unknowable - if we claim to know God then it is not God that we know said St Augustine. Any description will be inadequate and even Moses could not gaze upon the face of God.

***Slide 30 Buddhist***

Perhaps what we are doing is building a concept, projecting on to it attributes that are the best that we know such as justice, mercy, steadfast love, truth, compassion, charity, harmony, forgiveness and redemption, eternal life and even ultimate reality. The concept is not a reality in the scientific material sense that it can be measured, yet it is a powerful thing. A concept can profoundly affect human behaviour, it is hard to define precisely because by engaging with it we personalise it. We can add our own experience to the whole and draw on the experience of others in our personal quests for meaning, purpose and courage.

***Slide 31 churches etc***

Developing the concept of god provides a means of articulating some of our deepest insights in a way that can then be communicated to others through common language, ritual and myth and used as a practical guide to living, finding meaning and guiding choices. Regardless of whether this god exists apart from in human consciousness, at its best the practice of religion has provided a basis for ethics, a means of raising our aspirations, calming our fears and helping us to develop a purpose for living in almost every part of the world. It is a starting point for developing our own faith that, as we mature, will come to be based on our own inner experience. God that we encounter as **being** holds a different meaning for us than the naked, dominating, power of the physical universe. Our understanding of God provides a context in which we can develop and evaluate our own value systems involving all that we are - our intellect, our emotions and our hearts.

***Slide 32 Newman***

Our experience of God is, I think, deeper than I have suggested. When we experience something we choose to name God we may not be able to prove that we is communicating with any external reality, yet we can say that we understand that the universe beyond us is not empty of consciousness - deep communicates with deep. Or as Newman put it, **Cor ad cor loquitur** Heart speaks unto Heart. Many people pray unceasingly that the great heart of our own heart will still hold our vision

whatever befall. But note now how Newton's language and also mine is becoming less scientific and less precise than the earlier part of my talk. This is really important because inspirational experience is particular to the individual and to express. Furthermore, there needs to be space and flexibility in the language so we can relate to many insights from our own tradition and from others.

***Slide 33 Supernova***

***How can these insights inform and enrich our lives?***

The immense creative burst that is the Universe which has given birth to us is displayed in endless forms that inspire and delight us. We can only marvel at the vast power of matter and energy that combined to form everything from the stellar displays in the night sky to the unseen molecular machines that provide our cells with energy. Our universe is the manifestation of this creative force that in most religions provides a foundation for the concept of God.

***Slides 34-36 Chagall (3 slides)***

Humans are also filled with creative energy and we bring this to birth in any number of forms including * art, music, drama, science and literature. Innate biological systems control the mechanisms that sustain life, our cultural inheritance helps us to make the most of our environment, yet a truly original creative discovery by an individual is novel - it develops and is not pre-programmed or learned. * Once we become aware of new insights our impulse is to create something which will allow us to articulate our inner experience so that we can integrate it into our own lives and share it with others. This is not an easy process and we are continually challenged to bring our * informed and intuitive inner knowing to a reality that we can integrate into other forms of art or language to use as a platform of consolidated ideas from which to step further into the unknown.

***Slide 37 Rubilev***

An icon that to me addresses the way that intuitive understanding culminates in conscious knowing is the prefigurement of the Trinity in the visit of the three angels to Abraham by Rubilov. Painted by a man at prayer, this icon powerfully portrays the gentleness and strength of the relationships between the three angels or aspects of the Godhead, showing how each gives meaning to the others, sustains the others yet depends on them to achieve his own wholeness. The first angel represents that part of ourselves which is the root and ground and source of our being, the creator god whom, when we approach, creates a sense of awe in us as when we look into vast mountain ranges or deep into a starlit sky. The second angel, the human face of god encompassing justice, mercy, compassion and truth, represents that part of our being to which we have access, which we have struggled bring to conscious expression, articulating it first in music, symbol and the visual arts and finally in words. The third angel, wisdom, represents the way by which we synthesise conscious and unconsciously acquired information and then bring this holistic understanding to consciousness where we can act upon it.

***Slide 38 Zeldin***

These three aspects of our natures are inextricably woven together, for human beings have minds able to operate at the rational and scientific level as well as at the contemplative or imaginative level. Intuitive and rational interpretations of our human experience whether scientific, artistic or religious move through our levels of understanding to nurture and, once integrated, sustain our whole being in harmony.

***Slide 38 Dance***

There is no single entity in control of us. Not our genes, not our brains, not god. Every cell in our body has a completed copy of our genome and is sensitive to its own internal and external environment. There is no top down command system. Cells work in partnership with other cells around it. As we mature, we recognize that we are in a co-creative partnership with God. Attempts at total control exercised either by ourselves or by God may satisfy our desire for security, but it doesn't really

fit with our observance and experience of nature, or indeed with experience of ourselves at the level of intentional action. It appears, instead, that there is openness, a range of possibilities within nature. If either we envisage God as someone who designed everything once and for all at the beginning of creation, or we envision ourselves as the ultimate controllers of the natural world through science, then we need to take care that we do not preclude the possibility of creation itself being creative as it responds in harmony with changes to itself. Perhaps our understanding of God's involvement with us is such that together we can attain real novelty, contingency and opportunity that preserve the integrity of life in the process?

***Slide 39 Rugby***

To summarise then..

Human beings live in a glorious Technicolor world in which we are required to deal decisively with the messiness of everyday life on a minute by minute basis, despite the complexity of the information that both drives and informs us. We continually integrate simple information into more complex systems. Our most basic decisions are guided by the possibilities and limitations imposed by not only our genes but by many other molecules and by the environmen. The transcription factors that enable gene expression, the metabolic systems that supply our muscles with energy, the repair mechanisms that enable us to survive environmental insults and our immune systems that combat disease operate largely without any conscious intervention by us, according to principles that we increasingly understand.

***Slide 40 Isabella***

However, living a fulfilled human life is far more complicated than simply remaining alive. As individuals we need to become integrated into an even more complex world so that we can find a niche where we can flourish physically and emotionally. Our cultural environment teaches us how to relate to others, and gives us the practical skills and learning that we need to deal with the complex world of work and family.

***Slide 42 Hilary***

Yet most of us expect to achieve even more in the fleeting moment of consciousness that we are privileged to experience. Expressing our own particular creative ideas and responding to beauty, love, joy, sorrow, death and loss requires even more complex information and courage than our genes and culture alone can provide. This level of self expression that is uniquely our own arises from a synthesis that takes place deep within the human psyche;

***Slide 43 Stonehenge***

It culminates in an awareness of an environment that we grasp first as tenuously as a dream, which, even as it slips through our fingers, we struggle to articulate so that it can be of lasting value to ourselves and to others.

***Slide 44 St Paul***

So let us return to St Paul. Philippians 4:8

Finally, brethren, whatsoever things are true, whatsoever things are honest, whatsoever things are just, whatsoever things are pure, whatsoever things are lovely, whatsoever things of good report; if there be any virtue, and if there be any praise, think on these things.

Maybe in such an environment we will educate our genes.