



## Wholeness in Healthy Human Development

I believe that studying the normal processes of our body can provide important insights about ways that all the diverse members of humanity can lead healthy meaningful lives - as individuals and together as parts of larger communities. Biology offers helpful models of how diverse units can act harmoniously and cooperatively for the good of the greater whole. These models can accord belonging, meaning and dharma to the individual, while reminding us that we are part - small and significant - of one being and becoming.

Everyone begins life as one cell, which then undergoes rapid proliferation and diversification, until sufficiently mature to emerge as again one entity - one body, one person. Healthy body functioning depends upon harmonious interactions and clear communication among the many, many, very different individual units.

The one cell becomes the one body - a complex differentiated whole made up of ~37 trillion cells organized into the many different **organs systems** that function to sustain the human body. Each organ system in turn is composed of several different cell types, whose spatial relationships can vary in terms of homo/heterogeneity. Evolutionarily, increased diversity/complexity provides for increased capacity.

In a healthy body, the many constituent cells act in the best interests of the greater whole. Good **communication among the many differentiated parts** is needed for such healthy functioning. A variety of physiologic systems support whole-body coordination (e.g., nervous, blood, information-carrying molecules, structural tension).

In some organs, like brain and liver, information from the whole body is processed to determine optimal outgoing signaling - sending “messages” to other cells to let them know what the body is asking them to do. Information-carrying molecules can transmit their “message” to cells that express the receptors specific to that message; cells vary greatly in expression of these specific receptors and thus recognize different “messages”. Some cells may in turn secrete back information into the circulation.

Development generates this immense cellular diversity even as all the cells in one individual’s body contain the same coding instructions present in the originating one cell - the DNA code unique to that individual. Cells look and act so differently, because in any given cell, only part of the information contained in the whole DNA code is being used – the part needed to perform its own specialized functions. During **differentiation**, progressively more potential coding regions become inaccessible, honing the cell to put its energy into performing its particular role in the body. The well-being of the body as a whole is based upon each cell doing a good job of its own special role.

My suggestion is, when learning about the diverse functions and appearances of human cells and organ systems, to imagine yourself as a specialized cell, part of a larger organ system, a community of cells.



# The Diversity of Human Organ Systems and Cell Types

Every human body develops from one cell – the fertilized egg. While functioning as one integrated unit, each body is composed of a diversity of organ systems.

Each organ system is itself a community of varying combinations of several basic differentiated cell types. These multiple cell types perform distinct functions in a coordinated fashion, enabling that organ to make its specific contributions to the body as a whole.

Each of these basic cell types can be further subdivided into various subtypes – and so on – leading to fine levels of distinctions between even similar cell types.

Organs perform varying tasks for the body (often several tasks/organ system), for example:

Product synthesis

(e.g., liver, pancreas, thyroid, breast, pituitary...)

Information/communication/learning

(e.g., brain, nervous, immune, endocrine)

Transportation/movement

(e.g., blood, heart, musculature)

Metabolism/energy usage

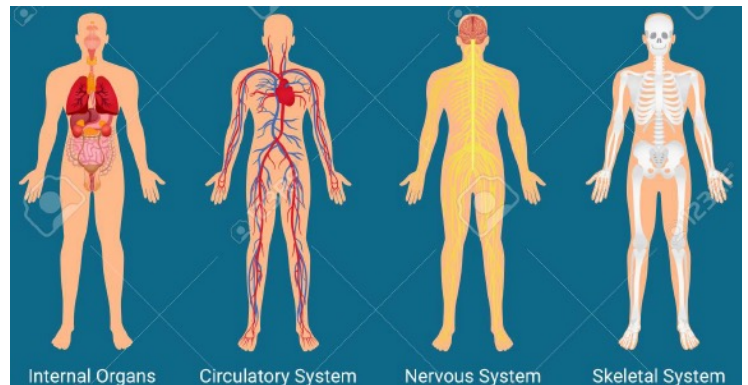
(e.g., liver, lung, thyroid, blood, intestine)

Reproduction (e.g. ovaries, testes, breast)

Structural/framing (e.g., bone, skin, musculature)

Self-protection (e.g., immune, blood, skin, adrenals)

Destruction/recycling/waste (e.g, liver, spleen, kidney, bladder)



Cell and tissue types:

**Connective** tissue cells - connect things together, providing physical structures, embedding matrix, padding, insulation, transportation and information channels

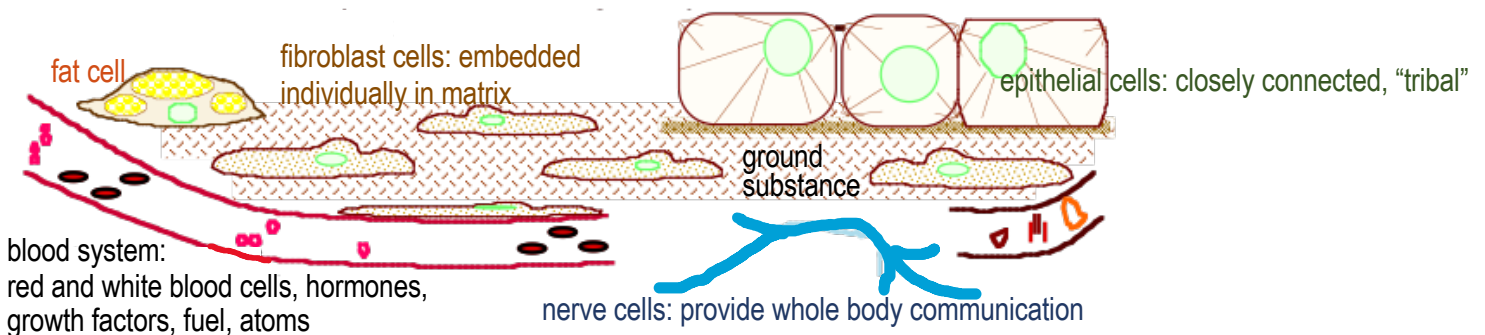
e.g., bone, nerve, fat, muscle, fibroblast

**Epithelial** cells – make and secrete specialized products and provide linings/boundaries/absorption

e.g., mammary makes milk products, thyroid and adrenals make hormones, bladder and endothelial provide lining, skin provides a boundary, lung and intestine absorb

**Blood** cells – e.g., red blood cells transport oxygen, white blood cells provide immune defense and scavenging

Inorganic **ground substance** (material exuded by cells) provides an organizational matrix

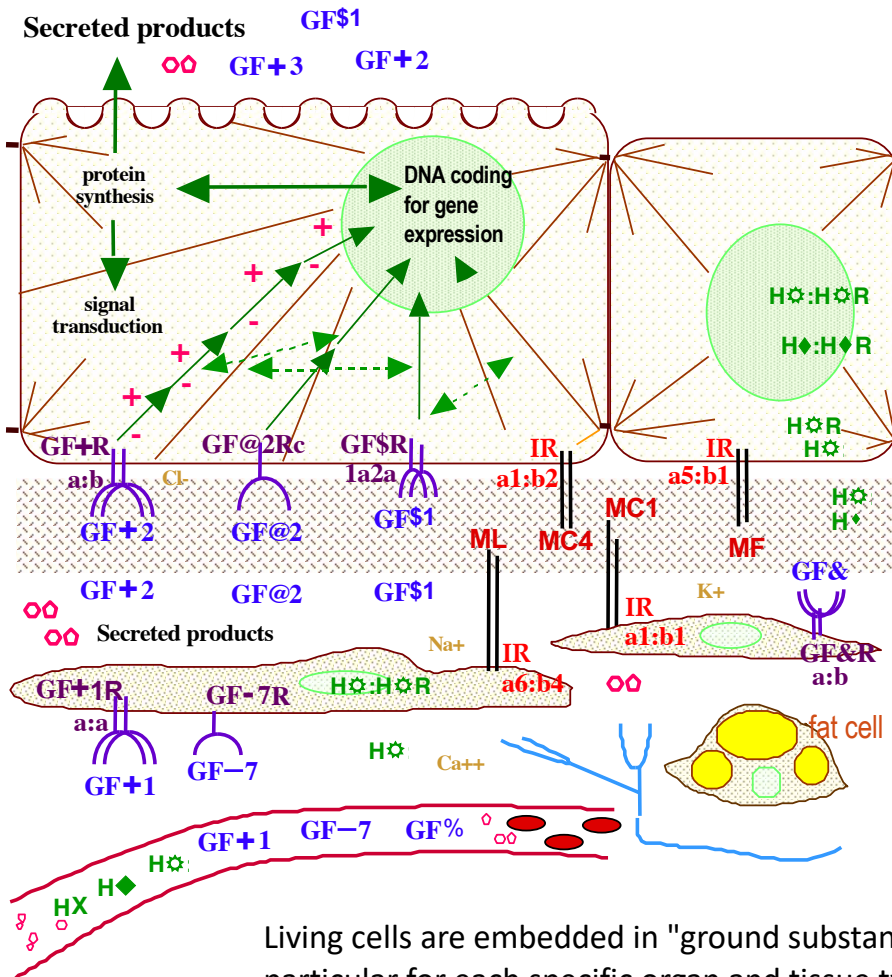


What kind of cell are you, what are your tasks, what is your calling, what are your specialized skills?  
To what larger "organ systems" do you belong; what is your role in them and what are their functions?

# Multi-Cellular Diversity, Multi-Messenger Communication

Many different information-carrying molecules are transmitted thru the whole body (blood systems) or are present in a local environment. Different cells perceive differing information. Based upon their particular tasks for the body, cells express a limited number of specific receptor molecules - and thus perceive only a limited amount of the information coursing thru the body. [like all the wireless information in our surroundings, which need an appropriate receptor (radio, TV, computer) to be perceived]  
 Healthy cells perceive accurately and act to the best of their ability.

## A REALLY simplified Model of multicellular diversity and communication in the breast



### Information-carrying messenger types

- GF:** growth factor (proteins)
- GF-R:** growth factor receptor (cell surface)
- H:** hormone (steroid, polypeptide)
- H-R:** hormone receptor (inside cell)
- M:** matrix molecule (proteins, sugars)
- IR:** integrins (matrix receptors) (transmembrane, also facilitate adhesion)

Complex interactive molecular "wiring systems" transmit information from outside the cell to the nucleus, determining which genes are expressed. This complexity provides cells with exquisitely sensitive responsiveness to environmental information.

Transmission and reception of information involves changes in structure, chemistry, and charge.

Living cells are embedded in "ground substance" matrices, whose composition is particular for each specific organ and tissue type. Cells do their specialized functions most effectively in their appropriate particular micro-environment.

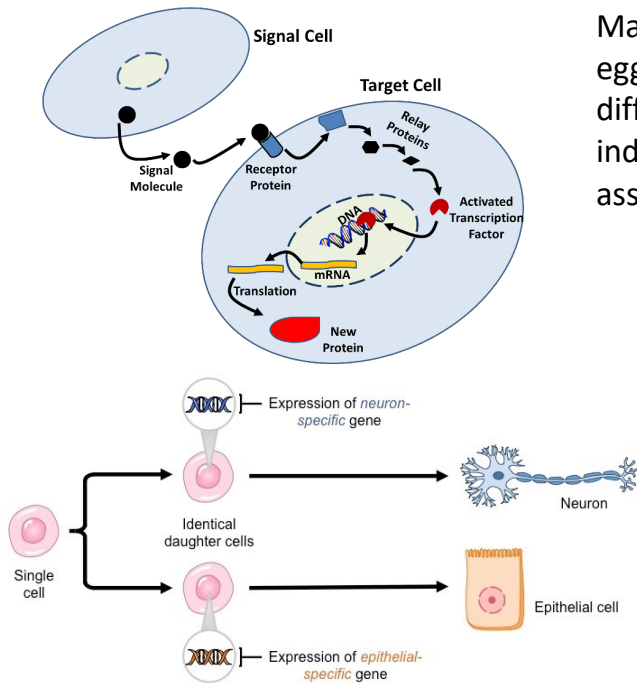
At both the molecular and cellular level, biology does mix-and-match - using a limited number of basic motifs to generate immense diversity of structure and function.

Constant motion and change, within the subparts and whole body, and the body and the whole of its environment in space and time, requires *dynamic* homeostasis to maintain balance.

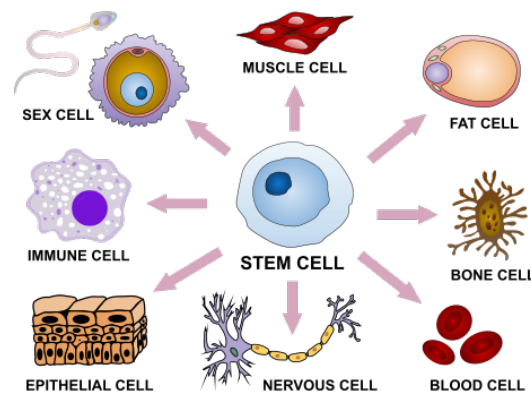
What kind of "receptors" do you recognize having? How similar/different do you think they are compared to other types of people?  
 Are there ways you can detect the presence of information in the environment, that you can't perceive directly, by its effects on others?

# Differentiation to Diversity by Limiting Expression

The fertilized egg is pluripotent – it can develop into every cell type in the body. As the embryo develops, the possible fates of a given cell become more and more limited. This is because expression of specific areas of the DNA that code for specialized functions become inaccessible to all but the particular cell types that need those functions to do their thing. Cells can vary greatly in the extent to which they do only limited specialized functions and or are able to do lots of different things.



Many mysteries remain about how exactly the one egg cell accurately differentiates into ~37 trillion different cells. It involves a limiting of the individual cell's capabilities so that it can effectively assume its destined role in the one body.



Although most cells in a mature human body are largely fixed into a differentiated (specialized/limited) fate, it's not impossible for some cells to revert to a pluripotent state – scientists have been able to do this under laboratory conditions, i.e., induced pluripotent cells

My image of what it means to be a cell in the body, a part of a greater whole .....

One wants to do the best one can at ones particular task,

while wishing that other cells also do the best they can ....

knowing that there are many different ways for cells to be, and that all together

they create a whole with greater complexity, capacity, and beauty.

We are cells and bodies on a path of evolution and maturation.

Consider: is there some part of your fate, calling, that you know in some deep way is part of your destiny, but has not yet been expressed?

Of possible interest: this past week one of the major science magazines (Science) had a whole section on new studies using new techniques, trying to more precisely identify the vast multitude of human cell types.

Some (slightly mashed together) excerpts from discussion of these 4 articles.

Our understanding of how cells form distinct tissues and organs and interact with each other is limited. Recent single-cell RNA sequencing analyses [looking at gene expression in individual cells] have described the landscapes of individual cell types, along with their abundance and interactions, in homeostasis and diseased conditions, but these studies are often limited to a single organ. A systematic comparison of cell types across different tissues is needed to understand shared and variable transcriptional features [what genes are expressed] and how these specializations are important for organ function. .... [they measured gene expression] in more than a million cells, including 500 cell types, across more than 30 human tissues from 68 donors. ...leading to the characterization of more than 400 cell types spanning epithelial, endothelial, stromal, and immune cell compartments.

... and profiled neuronal cells, muscle cells, and adipocytes, which are hard to dissociate and capture using scRNA-seq.

... examined the gene expression profile of more than 300,000 individual immune cells extracted from 16 different tissues in 12 deceased adult organ donors ... In-depth data analysis revealed insights into how the immune system adapts to function effectively in different organ contexts... Tissue-specific immune cell subsets emerged, with variable... tissue-residency features reflecting their adaptation to organ microenvironments.

These cross-tissue approaches recapitulated conserved cell-type features and revealed cell-state adaptations to distinct tissue environments. These data enable new insights into how the human genome parts list is used to create distinct cell types within the human organism. In addition to creating a detailed molecular definition of these cell types, the atlas reveals many other aspects of human biology, including how the same gene can be spliced differently in different cell types, how shared cell types in different tissues can have subtle differences in their identities, and how clones of the immune system can be shared across tissues.

For example, the Tabula Sapiens Consortium discovered that endothelial cells from lung, heart, uterus, liver, pancreas, fat, and muscle exhibit the most distinct transcriptional signatures, suggesting highly specialized functions, whereas endothelial cells from the thymus, vasculature, prostate, and eye resemble one another.