TITLE OF PROJECT: Creating a Kidney: How Stem Cells Might Be Used to Bioengineer a Vital Organ Regenerative Repair Stem Cell Kidney.

QUESTION: How might bioinformatic databases be used to determine the best protein environment for bioengineering a kidney, and how might stem cells be used to bioengineer vital organs?

VARIABLES:
Independent variable: Combination of soluble factors and ECM proteins
Dependent variable: Predicted efficiency of nephron differentiation
Possible constants: Species, databases, analysis method, criteria, integrin data

HYPOTHESIS: If I test different combinations of soluble signaling factors and ECM, then they result in different predicted levels of kidney cell differentiation, with combinations that share similar developmental roles and integrin interactions producing the strongest differentiation outcomes.
RESEARCH:

Organ Regeneration Through Stem Cells and Tissue Engineering https://pmc.ncbi.nlm.nih.gov/articles/PMC9973391/

Ajmal, L., Ajmal, S., Ajmal, M., & Nawaz, G. (2023). Organ regeneration through stem cells and tissue engineering. *Cureus*, *15*(1), e34336. https://doi.org/10.7759/cureus.34336
Facts:
1: The self-renewal ability of stem cells to differentiate into numerous lineages to assist in providing effective treatment for a range of injuries and diseases.
2: Regenerative engineering of organs or tissues represents an ever-expanding field that is aimed at developing biological replacements for dysfunctional organs or injured tissues.
3: The critical issue, however, with the engineering of organs outside the human body is the insufficient availability of human cells, the absence of a suitable matrix with the same architecture and composition as the target tissue, and the maintenance of organ viability in the absence of the blood supply.

4: The issue regarding the maintenance of the engineered organ viability can be solved using bioreactors consisting of media with defined chemical composition, i.e., nutrients, cofactors, and growth factors that can successively sustain the target cell's viability.

5: Stem cells are undifferentiated cells having self-renewal properties found in the body that can differentiate into different types of cells with specialized functions

6: Due to their pluripotency, differentiation, and self-regeneration properties, they have become important for the treatment of a wide variety of diseases that include traumatic brain injury, stroke, Alzheimer's disease, Parkinson's disease, spinal cord injury, deafness, baldness, blindness, wound healing, myocardial infarction, rheumatoid arthritis, osteoarthritis, muscular dystrophy, and diabetes.

7: Research in stem cells offers not only unprecedented opportunities for the development of new ways and systems of tackling diseases, but also paves the way for exploring fundamental questions and the needs of humans.

8: Along with the traditional hematopoietic stem cell technique, organ transplantation has also become clinically important for kidney or liver failure. However, the main obstacle in the organ transplantation program is the intense shortage of donor organs.

9: In the present era, researchers have been finding ways for the successful establishment of the whole organ using stem cells, some of which include the generation of the organ using a single adult tissue stem cell, a blastocyst complementation system, decellularization and recellularization of bio-scaffold, and a combinatorial technique employing stem cells and tissue engineering.

10: The recently introduced pluripotent stem cell technology is a successive advancement in the field of stem cell biology, as it allows the generation of pluripotent stem cells in patients from their own blood cells or skin cells. Induced pluripotent stem cells can then be reprogrammed to proliferate and produce high-quality mature cells for cellular therapy. Moreover, no stimulation of unwanted immunogenic reactions and no immunosuppression would be needed. Through this technology, patients suffering from organ failure and waiting for transplants can be helped.

What can I learn from this information to help me formulate a hypothesis?

I can learn that the human body is very adaptable in many remarkable ways.

Harvard University licenses kidney engineering. technology to Trestle Biotherapeutics

https://www.hsci.harvard.edu/news/harvard-licenses-kidney-engineering-technology-trestle

Harvard University licenses kidney engineering technology to Trestle Biotherapeutics | Harvard Stem Cell Institute (HSCI). (2022, February 28). https://www.hsci.harvard.edu/news/harvard-licenses-kidney-engineering-technology-trestle

Facts:

1: “More than a dozen members of my lab contributed to the innovations in tissue engineering that have created this technology platform,” said Lewis. “Most recently, we developed a new biomanufacturing method, known as sacrificial writing in functional tissue (SWIFT), that enables the fabrication of vascularized kidney tissues. I am pleased that Trestle has now launched to translate this robust technology to address the growing need for kidney tissues and organs.”
2: “We were able to demonstrate for the first time a more advanced kidney architecture and functionality in human kidney organoids, which is important for creating tissue segments for use in drug testing and disease modeling and, ultimately, in vivo therapeutics,” said Morizane. Lewis and Morizane are members of Trestle Biotherapeutics’ scientific advisory board.
3: The foundational technology was pioneered by researchers in the lab of Jennifer Lewis, who is a Wyss Core Faculty member, the Hansjörg Wyss Professor of Biologically Inspired Engineering at SEAS, and a Principal Faculty member at the Harvard Stem Cell Institute (HSCI).
4: Lewis’ lab has collaborated with several clinicians, including Ryuji Morizane, who is an assistant professor at Massachusetts General Hospital, an HSCI Affiliate Faculty member, and a Visiting Scholar at the Wyss, as well as Joseph Bonventre, an HSCI Executive Committee member at the Brigham.
5: The lack of transplantable kidney tissues and whole organs is a significant challenge in the treatment of chronic and end-stage kidney disease. As of 2021, in the U.S. alone, there are more than 550,000 dialysis-dependent patients and 100,000 patients waiting for kidney transplants, yet only about 20,000 transplants are performed each year, with nearly 5,000 patients on waiting lists dying each year without receiving a transplant.
6: Beyond kidney failure, there are more than 60 genetic diseases that directly or indirectly affect renal function, many of which cannot be appropriately treated with existing therapeutics.
7: A newly launched startup is building on innovations developed over several years at the Wyss Institute for Biologically Inspired Engineering at Harvard University, Harvard John A. Paulson School of Engineering & Applied Sciences (SEAS), and Brigham and Women’s Hospital (Brigham). San Diego-based Trestle Biotherapeutics has been granted a license by Harvard’s Office of Technology Development (OTD) to commercialize a suite of stem cell- and 3D bioprinting-based kidney regenerative medicine technologies.

8: Central to the success of this approach was a collaboration between the Lewis Lab and researchers at Brigham. Morizane, Bonventre, and other clinicians had developed a method for generating kidney organoids from human pluripotent stem cells in vitro.
9:These tissue constructs contained large numbers of well-organized nephrons, but lacked a vascular network that could be perfused with blood. This deficiency was overcome by subjecting the organoids to fluid flow through bioengineered devices. In a collaborative effort published in Nature Methods, the team succeeded in generating vascularized kidney organoids with enhanced nephron maturation in vitro.
10: “We are very excited to bring the biofabrication and stem cell biology technologies developed in the Lewis and Morizane labs into what we are building at Trestle. The teams at Harvard, Wyss, and Brigham have a renowned track record in translational innovation, and we are thrilled with the opportunity to carry their work forward for patients’ benefit,” said Ben Shepherd, the CEO of Trestle.

What can I learn from this information to help me formulate a hypothesis?

The info I can learn from this helps me formulate the hypothesis that this is one of the most important things we need in today's society to save lives.

Kidney Engineering Technology for New Tissue Replacement Therapies

https://wyss.harvard.edu/technology/kidney-engineering-technology-for-new-tissue-replacement-therapies/

Kidney engineering technology for new tissue replacement therapies. (2023, June 13). Wyss Institute. https://wyss.harvard.edu/technology/kidney-engineering-technology-for-new-tissue-replacement-therapies/

Facts
1: About 850 million people worldwide and 37 million people in the US suffer from kidney disease.
2: Currently, there are only two treatment options for people whose disease progresses to outright kidney failure – dialysis or a rare kidney transplant. While dialysis is a life-saving treatment for more than 550,000 Americans, patients must endure constant medical risks of infection, vascular collapse, and often severe tolls on their quality of life.
3: Kidney transplants are in extremely short supply: in the US alone, about 100,000 patients are waiting for a kidney transplant, yet, due to organ shortage, each year only 20,000 transplants are performed, and nearly 5,000 patients on waiting lists are dying.
4:Since the first patient was treated with repeated dialysis in 1960, and the first living-related kidney transplant was performed in 1954, no other treatments have been advanced to the clinic.
5:Key to the success of the Lewis team's human kidney engineering approach was their collaboration with clinical researchers Joseph Bonventre, M.D., Ph.D., Chief of the Division of Renal Medicine and Founding Chief of the Engineering in Medicine Division at the Brigham and Women's Hospital (Brigham), and Ryuji Morizane, M.D., Ph.D., an Assistant Professor at the Massachusetts General Hospital (MGH) and Harvard Medical School (HMS). Bonventre, Morizane, and others developed a method for generating kidney organoids from human pluripotent stem cells in culture dishes.
6: In 2020, Ben Shepherd, Ph.D., and Alice Chen, Ph.D., two research-entrepreneurs aiming to provide implantable therapeutic kidney tissue to patients, founded La Jolla-based Trestle Biotherapeutics.

7: Looking to complement their expertise in stem cell biology, tissue engineering, and regenerative medicine with additional methodology, they approached Lewis, Morizane, and other researchers to discuss the Harvard team's comprehensive kidney bioengineering capabilities.

8: In 2022, Trestle was granted a license to commercialize a suite of stem cell- and 3D bioprinting-based kidney regenerative medicine technologies created at the Wyss Institute, SEAS, and Brigham. Lewis is a member of Trestle's scientific advisory board.

9:In 2023, Trestle joined the Wellcome Leap HOPE program, which is focused on bioengineering complex human organs and immune system interactions, and helped Trestle advance the development of functional bioengineered kidney tissues.

10: The company will join a multi-disciplinary team being led by Lewis.

What can I learn from this information to help me formulate a hypothesis?

I learned that we all need to work together to help solve the world's problems.

Current Bioengineering Methods for Whole Kidney Regeneration

https://pmc.ncbi.nlm.nih.gov/articles/PMC4452081/

Yamanaka, S., & Yokoo, T. (2015). Current bioengineering methods for whole kidney regeneration. *Stem Cells International*, *2015*, 1–10. https://doi.org/10.1155/2015/724047

Facts:

1: Kidney regeneration is likely to provide an inexhaustible source of tissues and organs for immunosuppression-free transplantation.

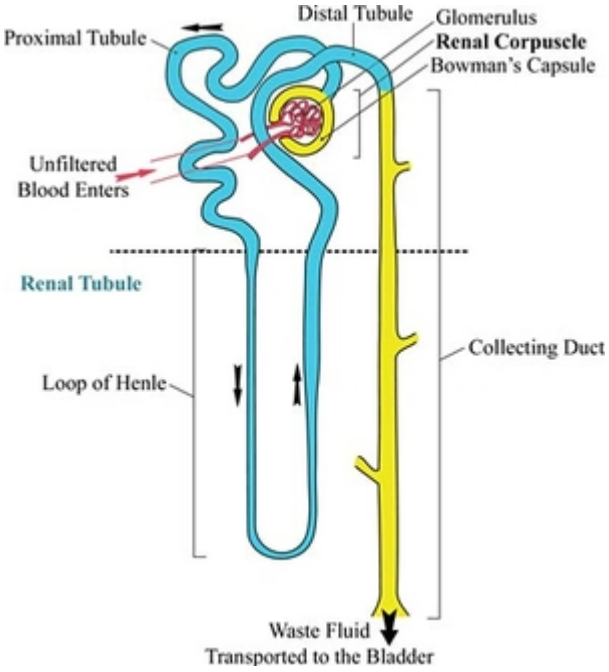
2: It is currently garnering considerable attention and might replace kidney dialysis as the ultimate therapeutic strategy for renal failure.

3: However, anatomical complications make kidney regeneration difficult. Here, we review recent advances in the field of kidney regeneration, including (i) the directed differentiation of induced pluripotent stem cells/embryonic stem cells into kidney cells; (ii) blastocyst decomplementation; (iii) use of a decellularized cadaveric scaffold; (iv) embryonic organ transplantation; and (v) use of a nephrogenic niche for growing xenoembryos for *de novo* kidney regeneration from stem cells.
4: All these approaches represent potentially promising therapeutic strategies for the treatment of patients with chronic kidney disease.
5: Although many obstacles to kidney regeneration remain, we hope that innovative strategies and reliable research will ultimately allow the restoration of renal function in patients with end-stage kidney disease.
6: Previous studies have suggested that pluripotent stem cells (PSCs) have the potential to differentiate into any cell type in the body and self-assemble into heterogeneous tissues or organs [4–6].
7: PSCs have indeed been shown to generate mature cells *in vitro*. PSCs therefore represent an important cell type for bioengineering strategies aimed at kidney regeneration.
8: PSCs include both embryonic stem cells (ESCs) and iPSCs. ESCs are derived from embryos and grown in primary culture [4], while iPSCs are produced from terminally differentiated cells using transfection factors such as c-myc, Oct4, Klf4, and Sox-2 [5, 6].
9: PSCs have been differentiated successfully into various types of cells and tissues, including intestine [7], hepatic [8, 9], neural [10, 11], hematologic [12], pancreatic [13, 14], and cardiac lineages [15].
10: This approach, whereby iPSCs or ESCs are differentiated into kidney or other progenitors, is termed “directed differentiation” and is accomplished by the sequential application of chemicals or growth factors.

What can I learn from this information to help me formulate a hypothesis?
I can learn that there are tons of things around that mimic our own environment and the functions of our body.

Similar Function	Factors
Differentiation + Development	Activin A, Wnt4, TGF-β
Cell Growth / Survival	IGF, PDGF, HGF
EMT Regulation	Activin A, Wnt4, TGF-β, HGF

Purpose of the Experiment: The purpose of my experiment is to help further learn about how to save the lives of those in need.



MATERIALS AND PROCEDURES

Materials:
Computer
Notebook
Spread sheat
internet

Definitions

Patient-specific
Tailored to an individual patient's biology, medical condition, genetics, or needs.

Bioengineering
Using engineering principles to solve problems in biology and medicine.

Regenerative medicine
A field focused on repairing, replacing, or regenerating damaged tissues or organs.

Stem cells
Cells that can divide and develop into different specialized cell types.

Synthetic scaffold
An artificial structure used to support growing cells in tissue engineering.

Nephrons
The basic functional units of the kidney are those that filter blood and form urine.

Renal corpuscle
The first part of the nephron, where blood filtration begins, includes the glomerulus and Bowman's capsule.

Glomerulus
A network of capillaries in the kidney that filters blood.

Bowman's capsule
A cup-shaped structure around the glomerulus that collects the filtered fluid.

Renal tubule
The tube extending from Bowman's capsule, where filtered fluid is processed into urine.

Differentiate
When a cell changes from a general cell type into a specialized one.

Human embryonic stem cells
Stem cells taken from early embryos can become any cell type in the body.

Pluripotent
Able to develop into almost any kind of cell in the body.

Human induced pluripotent stem cells (iPSCs)
Adult cells are reprogrammed back into a pluripotent (embryonic-like) state.

Immune rejection
When the immune system attacks transplanted cells, tissue, or organs, it does so because they are recognized as foreign.

Microenvironment
The local surroundings of a cell, including other cells, molecules, and physical conditions.

Cell media
The nutrient-rich liquid that cells grow in outside the body.

Substrate
The surface or material cells grow on or attach to.

Growth factors
Proteins that encourage cells to grow, divide, or differentiate.

Soluble factors
Molecules dissolved in the environment around cells that influence their behavior.

Extracellular matrix (ECM)
The structural network outside cells that provides support and signaling cues.

Cell receptors
Proteins on the cell surface that receive signals from outside the cell.

Bioinformatics
Using computers and software to analyze biological data (e.g., genes, proteins).

In vivo
Experiments or processes performed inside a living organism.

In vitro
Experiments are done outside the body, such as in a dish or test tube.

Signaling pathways
A series of molecular interactions inside a cell that control its behavior and responses.

Apoptosis
Programmed cell death is a regulated process by which cells self-destruct.

Epithelial-to-mesenchymal transition (EMT)
When epithelial cells change into mesenchymal (more mobile and flexible) cells, they are important in development, healing, and cancer.

Precursor cells
Partially specialized cells that can develop into specific mature cell types.

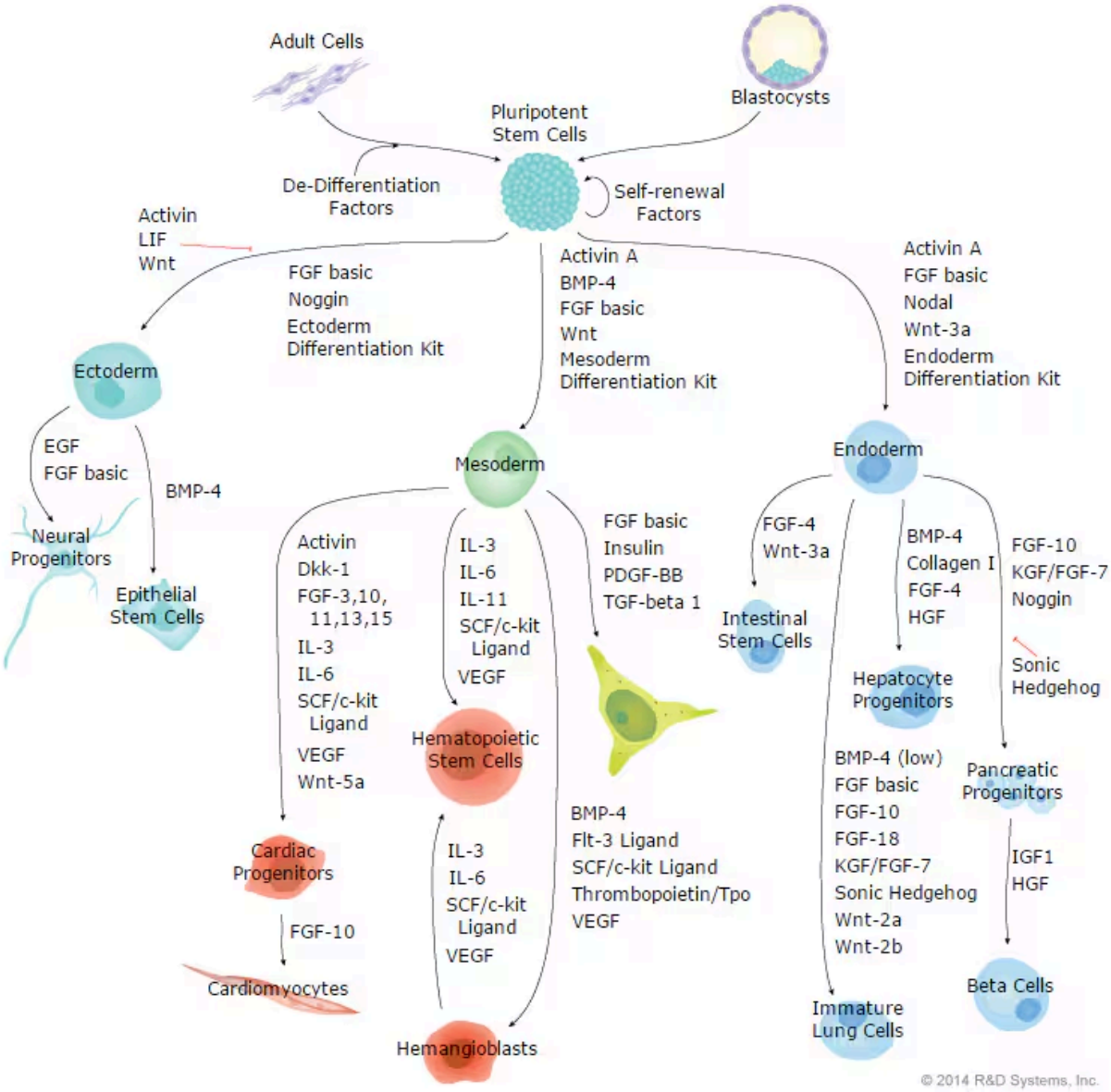
Integrins
Proteins on cell surfaces that help cells attach to the extracellular matrix and send signals inside the cell.

Microarray
A laboratory tool used to measure the activity (expression) of thousands of genes at once.

Procedures:

This experiment used bioinformatics databases and published research to predict outcomes rather than performing live-cell culture experiments.

Embryonic and Induced Pluripotent Stem Cell Differentiation Pathways & Lineage-specific Markers



SF EXPERIMENT DOCUMENTATION
(3 TRIALS)

TRIAL 1: DATE: 1/5/26

Time: 11:25 AM Beginning: 11:25 AM Ending: 1:00 PM (+1:45 hours)

Variables:

- Independent – Combination of soluble factors and ECM proteins
- Dependent – Predicted efficiency of nephron differentiation
- Controls – Species, databases, analysis method, criteria, integrin data

Procedures:

Soluble Factors Used

- Activin A
- Wnt4
- TGF-β

Shared Functions

- Differentiation and Development
- EMT Regulation

ECM Protein Selected

- Laminin-521

In Trial 1, soluble factors involved in kidney differentiation and development were selected based on shared biological functions. Activin A, Wnt4, and TGF-β were analyzed using Reactomes and confirming databases to verify their roles in nephron development and epithelial-to-mesenchymal transition (EMT).

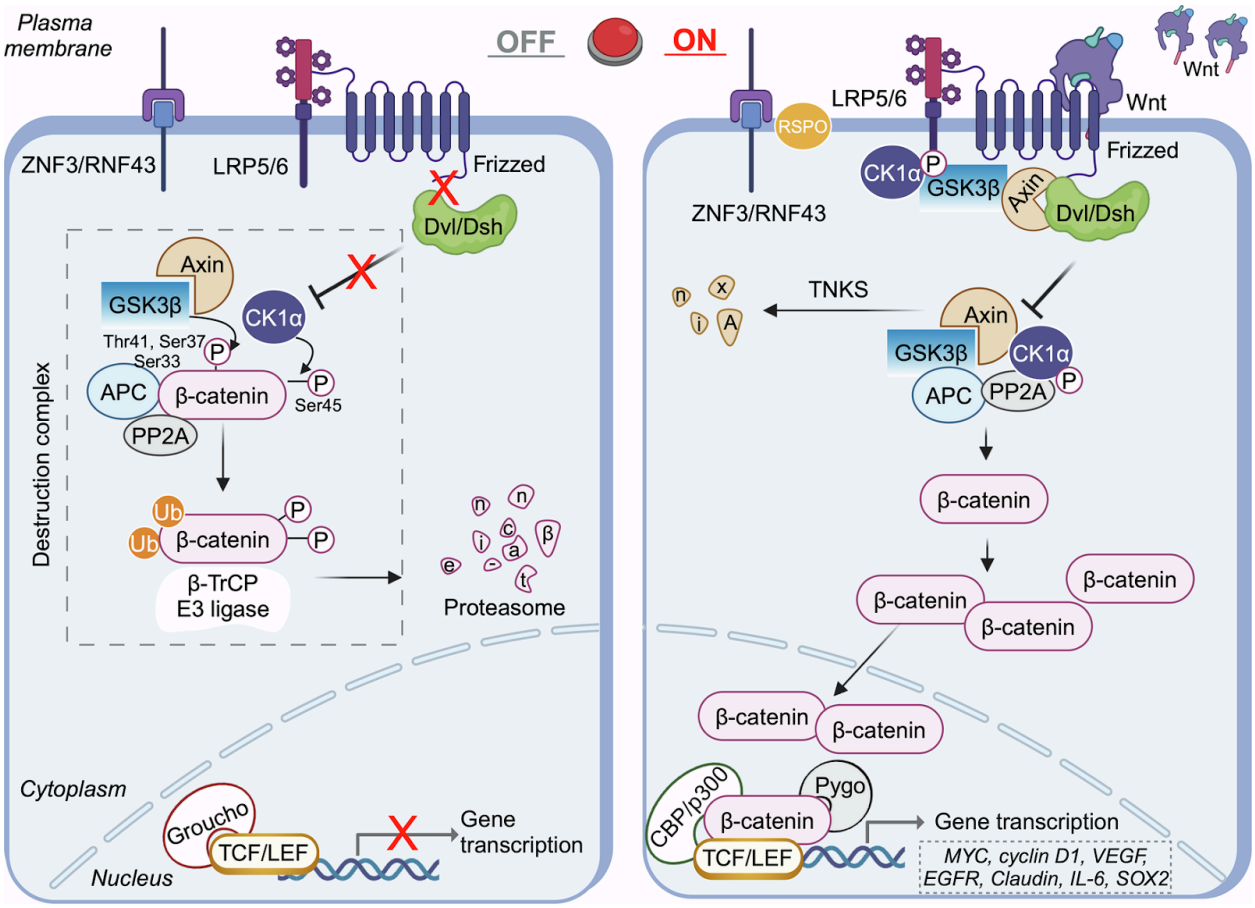
Integrin expression data from developing human kidney tissue were examined to identify integrins associated with nephron formation. Laminin-521 was selected as the ECM protein due to its known binding to kidney-expressed integrins. All pathway, integrin, and ECM information was recorded in tables for later comparison.

Results of Trial 1 experiment were:

The pathway analyses showed substantial overlap in differentiation and development signaling. Laminin-521 binds integrins expressed in early nephron cells, supporting predicted nephron differentiation.

Observations/ thoughts from my experiment: This combination demonstrates strong coordination between developmental and EMT signaling and highlights the importance of matching soluble factors to compatible ECM proteins for nephron structure.

My expectation was that …. As I predicted, selecting soluble factors with shared roles in differentiation, development, and EMT regulation, paired with an ECM protein compatible with kidney integrins, would yield a biologically reasonable condition for nephron differentiation.



TRIAL 2: DATE: 1/5/26

Time: 1:30 Beginning: 1:30 Ending: 2:45 +1:15 hour

Variables:

- Independent – Combination of soluble factors and ECM proteins
- Dependent – Predicted efficiency of nephron differentiation
- Controls – Species, databases, analysis method, criteria, integrin data

Procedures:

Soluble Factors Used

- IGF
- PDGF
- HGF

Shared Functions

- Cell Growth and Survival
- EMT Regulation (HGF)

ECM Protein Selected

- Fibronectin

In Trial 2, soluble factors primarily involved in cell growth and survival were selected to evaluate a different signaling emphasis. IGF, PDGF, and HGF were analyzed for their involvement in pathways related to proliferation, survival, and EMT regulation.

Integrin expression data were reviewed to identify integrins commonly associated with mesenchymal and proliferative signaling environments. Fibronectin was selected as the ECM protein due to its strong association with integrin-mediated growth signaling. Data were recorded in the same tables and analyzed using the same criteria as in Trial 1.

Results of the Trial 2 experiment were:

The analyses predicted strong growth and survival signaling, while EMT regulation was present but less integrated with developmental pathways. Fibronectin binds integrins involved in growth-supportive signaling.

Observations/ thoughts from my experiment :
This combination favors proliferation and survival of precursor nephron cells and represents a general growth-supportive environment.

I expected that… A result of this trial was that growth- and survival-related soluble factors paired with a compatible ECM protein would constitute a distinct differentiation environment compared to development-focused conditions.

TRIAL 3: **DATE: 1/5/26**

Time: 3:00 Beginning: 3:00 Ending: 4:00 +1:00 hour

Variables:

- Independent – Combination of soluble factors and ECM proteins
- Dependent – Predicted efficiency of nephron differentiation
- Controls – Species, databases, analysis method, criteria, integrin data

Procedures:

Soluble Factors Used

- Activin A
- Wnt4
- HGF

Shared Functions

- Differentiation and Development
- EMT Regulation

ECM Protein Selected

- Collagen IV

In Trial 3, soluble factors were selected to combine developmental signaling with EMT regulation. Activin A and Wnt4 provided developmental signaling, while HGF contributed to EMT-related regulation. Pathway involvement was confirmed using the same databases and criteria as previous trials.

Integrin expression data were examined to identify ECM compatibility, and Collagen IV was selected due to its abundance in kidney basement membranes. All findings were documented for comparison across trials.

Results of the Trial 3 experiment were:

Pathway analyses predicted moderate differentiation efficiency with a balance of developmental and EMT regulation. Collagen IV binds kidney-expressed integrins to support the structural organization of the kidney.

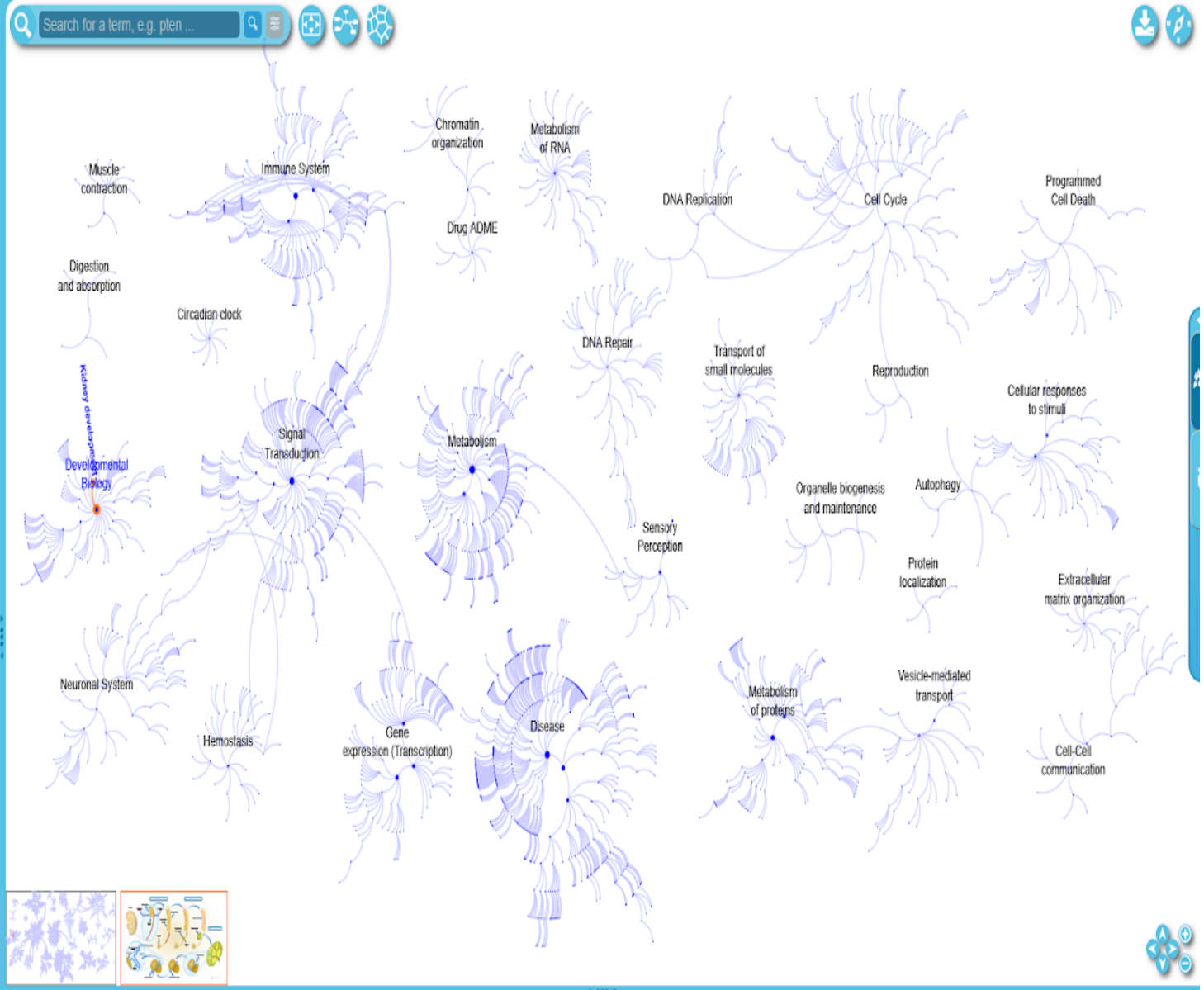
Observations/ thoughts from my experiment :
This combination balances differentiation and EMT signals, creating a predicted environment for precursor nephron cells poised for differentiation.

My expectation was that …. The conclusion was that combining developmental and EMT-regulating soluble factors with a kidney basement membrane ECM protein would create a biologically relevant differentiation condition distinct from those in Trials 1 and 2.

Event Hierarchy:

- Autophagy
- Cell Cycle
- Cell-Cell communication
- Cellular responses to stimuli
- Chromatin organization
- Circadian clock
- **Developmental Biology**
  - Maternal to zygotic transition (MZT)
  - Transcriptional regulation of pluripotent stem cells
  - Gastrulation
  - Signaling by NODAL
  - Activation of HOX genes during differentiation
  - Nervous system development
  - LGI-ADAM interactions
  - Myogenesis
  - Cardiogenesis
  - **Kidney development**
  - Regulation of beta-cell development
  - Transcriptional regulation of testis differentiation
  - Keratinization
  - Transcriptional regulation of granulopoiesis
  - Developmental Cell Lineages
  - MITF-M-regulated melanocyte development
  - Adipogenesis
  - Differentiation of T cells
- Digestion and absorption
- Disease
- DNA Repair
- DNA Replication
- Drug ADME
- Extracellular matrix organization
- Gene expression (Transcription)
- Hemostasis
- Immune System
- Metabolism
  - Metabolism of carbohydrates and carbohydrate derivatives
  - Inositol phosphate metabolism
  - Metabolism of lipids
  - Integration of energy metabolism
  - Metabolism of nitric oxide: NOS3 activation and regulation

Search for a term, e.g. pten ...



Description | Molecules | Structures | Expression | Analysis | Downloads

Kidney development | Id: R-HSA-9830369.1 | Species: Homo sapiens | Review Status: 3/5

Summation

Kidney development begins at embryonic day 8.5 (E8.5) in mouse embryos, a time after gastrulation and formation of the intermediate mesoderm (reviewed in Marcotte et al. 2014, Smyth 2021, Schnell et al. 2022). Renal progenitors are specified within the intermediate mesoderm in the region between the 6th and 8th somites. The nephric duct then begins to form by mesenchymal to epithelial transitions of the renal progenitors and grows caudally to fuse with the bladder and urethra primordium (cloaca). The nephric duct induces the formation of mesonephric tubules in the adjacent nephric cord which form the mesonephros, an embryonic kidney in mammals that regresses and is supplanted by the metanephros. (In anamniotes such as frogs and fish, the mesonephros is the adult kidney and no metanephros forms.)

In mammals, the metanephros is initiated as the caudal region of the nephric cord forms metanephric mesenchyme which then interacts with the nephric duct to induce formation of the ureteric bud, the progenitor of the ureter. Branching of the ureteric bud forms ureter tips which induce nephron formation in the surrounding metanephric mesenchyme (reviewed in El-Dahr et al. 2008, O'Brien and McMahon 2014, Desgrange and Cereghini 2015, Chambers and Wingert 2020, Schnell et al. 2022).

Induction of kidney development in the intermediate mesoderm occurs by incompletely characterized signals from the adjacent ectoderm and lateral plate mesoderm. Notably, BMP activity from the lateral plate mesoderm can induce

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Genes, MANE Project (release v1.5)
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Data Chart and Graphs

Soluble factor	Abbreviated gene name	Family it belongs to	Does it regulate proliferation or apoptosis?*	Does it regulate differentiation ?	Does it regulate development?	Does it regulate epithelial-to-mesenchymal transition?**	What other key functions does it have?
Activin A	INHBA	The TGF-beta family of growth factors controls tissue formation by inhibiting growth and is also a family of hormones involved in human reproduction. “	“Activin A significantly inhibited the proliferation of human thyroid follicular epithelial cells in vitro in concentrations between 0.5 and 50 ng/ml and was almost as potent as TGFbeta-1. “	“No. It says Activin A regulates proliferation (cell growth inhibition), not differentiation. “	“It indicates Activin A is involved in tissue formation (a developmental process), but the study itself focuses on regulating cell proliferation in adult thyroid tissue, not the development of the thyroid. “	Not necessarily. It says, “ It is elevated in myeloma patients with advanced disease and correlates with adverse disease features, extensive bone disease, and poor prognosis (Terpos et al., 2012). Sotatercept is an activin-A inhibitor, which was administered in patients with MM in a phase 2 study	“The role of activin A during the inflammatory response is unclear, because it appears to have both pro- and anti-inflammatory actions, as defined by its effects on cytokine production. Studies in sheep have shown that systemic levels of activin A increase very rapidly in response to an inflammatory

						and showed that it could probably increase bone mineral density (Abdulkadyrov et al., 2014)."	stimulus, and concentrations peak before those of the early-response proinflammatory mediator tumor necrosis factor α."
Retinoic acid	RARA	"The retinoids are a group of compounds including vitamin A and its active metabolite, all-trans-retinoic acid (ATRA). "	"They support apoptosis. While the reverse transformation of retinaldehyde to retinol is possible through the DHRS3 enzyme activity, the retinaldehyde to RA conversion is irreversible."	Yes. "Retinoids regulate a variety of physiological functions in multiple organ systems, are essential for normal immune competence, and are involved in the regulation of cell growth and differentiation ."	Yes. "Retinoic acid receptors are key developmental regulators and, as such, function as a molecular switch in many developmental processes, including skin development. In the absence of a ligand, RARs repress transcription by recruiting histone deacetylase (HDAC) complexes,	Yes. "Retinoids are involved in the process of embryogenesis during the development of the nervous system, liver, heart, kidneys, intestine, eyes, and limbs. Retinoids are used in the treatment of the so-called "night blindness" because they are responsible	" They are used in the pharmacotherapy of diseases such as acne and rosacea, psoriasis, cancer, inflammation of hair follicles with bacterial aetiology, pyoderma, lupus erythematosus, and ichthyosis."

					such as HDAC-N-CoR (negative co-repressor) or HDAC-SMRT (silencing mediator for retinoid and thyroid hormone receptors). “	for the proper functioning of the organ of sight.”	

Wnt4	WNT4	“The WNT4 gene family consists of structurally related genes which encode secreted signaling proteins.”	It regulates both apoptosis and proliferation. “ These proteins have been implicated in oncogenesis and in several developmental processes, including regulation of cell fate and patterning during embryogenesis. “	Yes. “This gene is a member of the WNT gene family, and is the first signaling molecule shown to influence the sex-determination cascade. It encodes a protein which shows 98% amino acid identity to the Wnt4 protein of mouse and rat.“	Yes. This gene and a nuclear receptor known to antagonize the testis-determining factor play a concerted role in both the control of female development and the prevention of testes formation.”	In certain circumstances, yes. “ This gene and another two family members, WNT2 and WNT7B, may be associated with abnormal proliferation in breast tissue. Mutations in this gene can cause Rokitansky-Kuster-Hauser syndrome and SERKAL syndrome. [provided by RefSeq, Jul 2008].”	“ A homozygous missense mutation in WNT4 in humans that results in greatly reduced WNT4 mRNA expression is associated with renal agenesis, gonadal defects, and adrenal hypoplasia from 19 weeks’ gestation (Mandel et al., 2008), and Wnt4-null mice demonstrate impaired kidney development from 15 dpc (Stark et al., 1994) along with defects of the female reproductive

							system (Vainio et al., 1999), Sertoli cell differentiation in the testes (Jeays-Ward, Dandonneau, & Swain, 2004), and adrenal glands with reduced CYP11B2 expression and Pref-1/Dlk1 expression (Heikkila et al., 2002)."

Hepatocyte growth factor	HGF	“While HGF was discovered in the sera of 70%-hepatectomized rats, 5) The c-Met proto-oncogene product (c-Met) had been identified as a new member of the tyrosine kinase family, possibly as a new receptor of unknown growth factor(s): Bottaro et al.”	It regulates proliferation. This factor stimulated DNA synthesis and proliferation of adult rat hepatocytes in primary culture, and we named it “Hepatocyte growth factor” or “Hepatotropin”. 5) Our in vitro assay system also contributed to the “complete purification” of rat HGF from the platelets of 3,000 rats and revealed that it was a new growth factor. 6,7)”	Yes, “ In fetal stages, HGF-neutralization, or c-Met gene destruction, leads to hypoplasia of many organs, indicating that HGF signals are essential for organ development. Endogenous HGF is required for self-repair of injured livers, kidneys, lungs, and so on.”	Yes, “ In addition, HGF exerts protective effects on epithelial and non-epithelial organs (including the heart and brain) via anti-apoptotic and anti-inflammatory signals.”	Yes	“ HGF has multiple biological functions, required for the generation, development, and maturation of parenchymal organs, as shown in Fig. 1B. HGF is expressed mainly by mesenchymal cells, while c-Met is identified on the parenchyma during organogenesis, 20,65,66) suggesting that HGF-c-Met signals play an essential role in mammalian and non-mammali

							an developments .”
Transforming growth factor alpha	TGFA	“ Transforming growth factor-alpha (TGF-α, TGFA) was the second member of the EGF receptor (EGFR) ligand family to be identified after the discovery of the prototypic member, EGF.”	Proforms apoptosis. TGFA activity was first discovered when researchers observed that sarcoma virus-transformed fibroblasts released a peptide growth factor that could block EGF binding to cells, suggesting that another growth factor competed with EGF for binding to cell-surface EGFRs.	In some ways, yes and no. Several detailed radiolabeling and pulse-chase experiments using different tagged and untagged TGFA constructs in various cell lines have shown consensus biosynthesis and processing of TGFA. “	“In the second study, human TGFA cDNA was cloned under the mouse metallothionein Ie promoter. All of the transgenic mice displayed interstitial fibrosis and acinar-ductular metaplasia of the pancreas. These transgenic mice also showed reduced ability of the mammary glands to penetrate fat pads. Multifocal yet well-differentiated	In some ways, yes, yes. However, hyperplasia was only observed after 4 months of age, when the mice reached puberty, suggesting that hormonal changes might affect TGFA signaling, consistent with another study that reported hyperplasia in postlactational mammary glands [31].	“Much has been learned about the role of TGFA in normal and disease states from mouse models in which TGFA/Tgfa has been overexpressed or knocked out. These studies, combined with other mechanistic studies, show that TGFA is involved in several cellular signaling pathways. Some of these actions are summarized in Table 1, which shows that different

					neoplasms of the liver were observed with a high degree of penetrance [32]. Pancreatic transformation was also recapitulated in pancreas-specific TGFA transgenic mice subsequently developed [33, 34]. “		stimuli affect TGFA levels, localization, and activity, indicating that TGFA is an important integrator of cellular signaling and function. A common action of TGFA is increased proliferation, driven by activation of EGFR downstream signaling. Still, it may also mediate other functions, such as mucous production and gastric acid secretion inhibition, as seen in overexpression models that mimic

							Ménétrier's disease. Below, we will discuss the phenotypes and information gathered from these studies."
Transforming growth factor beta	TGFB1	"This gene encodes a secreted ligand of the TGF-beta (transforming growth factor-beta) superfamily of	"This encoded protein regulates cell proliferation."	"This encoded protein regulates cell proliferation, differentiation , and growth, and can modulate the expression	"This encoded protein regulates cell proliferation, differentiation , and growth, and can modulate the expression	"This encoded protein regulates cell proliferation, differentiatio n, and growth, and can modulate	"Broad expression in spleen (RPKM 38.0), bone marrow (RPKM 32.1), and 23 other tissues."

		proteins. Ligands of this family bind various TGF-beta receptors, leading to recruitment and activation of SMAD family transcription factors that regulate gene expression."		and activation of other growth factors, including interferon gamma and tumor necrosis factor alpha. This gene is frequently upregulated in tumor cells, and mutations in this gene result in Camurati-Engelmann disease."	and activation of other growth factors, including interferon gamma and tumor necrosis factor alpha. This gene is frequently upregulated in tumor cells, and mutations in this gene result in Camurati-Engelmann disease."	the expression and activation of other growth factors, including interferon gamma and tumor necrosis factor alpha. This gene is frequently upregulated in tumor cells, and mutations in this gene result in Camurati-Engelmann disease."	
Insulin-like growth factor	IGF1	" Insulin-like growth factor-1 (IGF-1) belongs to a small family of secreted single-chain polypeptides that play important	"Because these factors play pivotal roles in cellular proliferation, differentiation, and function, they are tightly regulated at	Yes, "IGF-1 plays a pivotal role in fetal development, adolescent growth, and adult tissue homeostasis. Together with insulin and GH, IGFs	"Animal models of IGF deficiency have confirmed its critical role in embryogenesis and postnatal growth. IGF-1 null mice	"Likewise, IGF-1 receptor null mice weigh 55% of wild-type littermates and die within a few hours after birth because of	"IGF-1 exerts its effects on skeletal acquisition in an endocrine and autocrine/para-crine manner. Studies from inbred mouse

		roles in growth, development, and metabolism. This family includes proinsulin, insulin, IGF-1, and IGF-2, which show high amino acid sequence homology and share a similar ternary structure.”	the transcriptional and posttranscriptional levels.”	regulate glucose and lipid metabolism and thereby regulate body composition. Imbalance in IGF production or function is associated with various pathologic conditions, including short stature, insufficient skeletal acquisition, alterations in body composition (lean and fat mass), impairments in reproduction, reduced mental and physical capacity associated with aging, and metabolic	show marked growth retardation in utero and postnatally. These mice are 65% of normal weight at birth, and most die shortly after birth. 21–23 Survivors do not undergo a peripubertal growth spurt and have only 30% of the body weight of wild-type animals as adults. IGF-2 null mice are also growth-impaired, but their growth retardation occurs exclusively in utero, whereas postnatal growth is	respiratory failure. These mice show organ hypoplasia, 21 lung, skin, bone, and neurologic defects. 21,23 Taken together, the IGF-1R null mice established this receptor as an essential regulator of organogenesis. Contrary to models of IGF deficiency, IGF-1 transgenic mice showed significant increases in body weight and organomegaly caused by tissue hyperplasia.”	strains showed correlations between serum IGF-1 levels and skeletal acquisition. Mouse strains with low IGF-1 (C57BL/6J) have reduced total BMD and cortical thickness, whereas mice with higher serum IGF-1 levels (C3H/HeJ) show increased total BMD and femoral cortical thickness.”

				disorders.”	expected. 21 indicating that in mice only IGF-1 is critical postnatally.”		
Platelet-derived growth factor	PDGFA	“Today, the PDGF family of growth factors consists of five different disulphide-linked dimers built up of four different polypeptide chains encoded by four different genes. These isoforms, PDGF-AA, PDGF-AB,	Apoptosis “The classic PDGFs, PDGF-A and PDGF-B, undergo intracellular activation during transport in the exocytic pathway for subsequent secretion, while the novel PDGFs, PDGF-C and PDGF-D, are	Yes, “ The classical PDGF polypeptide chains, PDGF-A and PDGF-B, are well studied, and they regulate several physiological and pathophysiological processes, mainly using cells of	Yes, “The classical PDGF polypeptide chains, PDGF-A and PDGF-B, are well studied, and they regulate several physiological and pathophysiological processes, mainly using cells of	In some situations.	“The classical PDGF polypeptide chains, PDGF-A and PDGF-B, are well studied, and they regulate several physiological and pathophysiological processes, mainly using cells of mesenchymal

		PDGF-BB, PDGF-CC, and PDGF-DD, act via two receptor tyrosine kinases, PDGF receptors alpha and beta."	secreted as latent factors that require activation by extracellular proteases."	mesenchymal or neuroectodermal origin as their targets."	mesenchymal or neuroectodermal origin as their targets."		or neuroectodermal origin as their targets. The discovery of two additional ligands for the two PDGF receptors suggests that PDGF-mediated cellular signaling is more complex than previously thought."

Soluble factor	Abbreviated gene name	Family it belongs to	Does it regulate proliferation or apoptosis?*	Does it regulate differentiation?	Does it regulate development/kidney growth?	Does it regulate epithelial-to-mesenchymal transition (EMT) ?**	What other key functions does it have?
Activin A	INHBA	This gene encodes a member of the TGF-beta (transforming growth factor-beta) superfamily of proteins.	Yes - inhibits proliferation	Yes, it plays a role in the development of the eye, tooth, and testis.	Broad expression in endometrium (RPKM 12.3), gall bladder (RPKM 11.3), and 15 other tissues, including the kidney. Required for early nephron formation.	Yes, elevated expression of this gene may be associated with cancer cachexia in human patients.	Stem cell maintenance, patterning
Retinoic acid	RARA	This gene represents a nuclear retinoic acid receptor. The encoded protein, retinoic acid	This gene has been implicated in the regulation of development, differentiati	Yes	Ubiquitous expression in lung (RPKM 10.4), spleen (RPKM 8.4), and 25 other	Yes, translocations between this locus and several other loci have been associated with acute	Controls cell fate decisions

		receptor alpha, regulates transcription in a ligand-dependent manner.	on, apoptosis, granulopoiesis, and transcription of clock genes.		tissues, including the kidneys. Needed for Kidney patterning and maturation.	promyelocytic leukemia. Alternatively spliced transcript variants have been found for this locus.	
Wnt4	WNT4	The WNT gene family consists of structurally related genes that encode secreted signaling proteins.	These proteins have been implicated in oncogenesis and in several developmental processes, including the regulation of cell fate and embryonic patterning.	Yes	Biased expression in skin (RPKM 8.0), ovary (RPKM 4.5), and 13 other tissues, including the kidney. Needed for driving renal tubule formation.	Yes, this gene and two other family members, WNT2 and WNT7B, may be associated with abnormal breast tissue proliferation. Mutations in this gene can cause Rokitansky-Kuster-Hauser syndrome and SERKAL syndrome.	Cell signaling and polarity

Hepatocyte growth factor	HGF	This gene encodes a protein that binds to the hepatocyte growth factor receptor to regulate cell growth, cell motility, and morphogenesis in numerous cell and tissue types.	Promotes apoptosis, alternative splicing results in multiple transcript variants, at least one of which encodes a preproprotein that is proteolytically processed to generate alpha and beta chains, which form the mature heterodimer.	This protein is secreted by mesenchymal cells and acts as a multi-functional cytokine on cells of mainly epithelial origin. This protein also plays a role in angiogenesis, tumorogenesis, and tissue regeneration. So yes	Biased expression in the placenta (RPKM 90.6), adrenal (RPKM 7.0), and two other tissues, including the kidney. It is needed for tubule growth and branching.	Although the encoded protein is a member of the peptidase S1 family of serine proteases, it lacks peptidase activity. Mutations in this gene are associated with nonsyndromic hearing loss.	Cell migration, tissue repair
Transforming growth factor alpha	TGFA	This gene encodes a growth factor that acts as a ligand for the epidermal growth	It performs proliferation	Yes	Yes, it is needed for general organ development.	This gene has been associated with many types of cancers, and it may also be involved in some	Cell growth signaling

		factor receptor, which activates signaling pathways for cell proliferation, differentiation, and development.				cases of cleft lip/palate.	
Transforming growth factor beta	TGFB1	This gene encodes a secreted ligand of the TGF-beta (transforming growth factor-beta) superfamily.	This encoded protein regulates cell proliferation, differentiation, and growth, and can modulate the expression and activation of other growth factors, including interferon	Yes	Broad expression in spleen (RPKM 38.0), bone marrow (RPKM 32.1), and 23 other tissues, including the kidneys, and regulates nephron differentiation.	This gene is frequently upregulated in tumor cells, and mutations in it cause Camurati-Engelmann disease.	Apoptosis, fibrosis

			gamma and tumor necrosis factor alpha.				
Insulin-like growth factor	IGF1	The protein encoded by this gene is similar to insulin in function and structure and is a member of a family of proteins that mediate growth and developmen t.	apoptosis	Yes	Broad expression in endometriu m (RPKM 7.0), fat (RPKM 6.3), and 18 other tissues, including the kidneys, supports kidney growth.	The encoded protein is processed from a precursor, binds a specific receptor, and is secreted. Defects in this gene cause insulin-like growth factor I deficiency. Alternative splicing results in multiple transcript variants encoding different isoforms that may undergo similar	Metabolism, survival

						processing to generate mature protein.	
Platelet-derived growth factor	PDGFA	This gene encodes a member of the protein family comprised of both platelet-derived growth factors (PDGF) and vascular endothelial growth factors (VEGF).	The encoded preproprotein is proteolytically processed to generate platelet-derived growth factor subunit A, which can homodimerize or heterodimerize with platelet-derived growth factor subunit B.	Yes	Ubiquitous expression in lung (RPKM 8.8), placenta (RPKM 8.7), and 24 other tissues, including the kidneys and mesenchymal development.	These proteins bind and activate PDGF receptor tyrosine kinases, which play a role in a wide range of developmental processes—alternative splicing results in multiple transcript variants.	Cell migration

Nephron Cell Type	Main Supplemented Soluble Factors	Research Paper
Renal Corpuscle Cells: Podocytes in the Glomerulus	No factors added	Kramer et al., 2005
	• Activin A • Retinoic acid (RA) • Conditioned media**	Ren et al., 2010
Renal Tubule Cells	No factors added	Kramer et al., 2005

	• Wnt4* • hepatocyte growth factor (HGF) • Activin A	Kobayashi et al., 2005
	Activin A	Morizane et al., 2009
Necessary for General Kidney Development	• Transforming growth factor (TGF) alpha • Transforming growth factor (TGF) beta • Insulin-like growth factor (IGF) • Platelet-derived growth factor (PDGF)	Dankers et al., 2011

α Integrin Subunits	β Integrin Subunits	ECM Proteins: They Bind
α2	β1	Laminin-111, Laminin-211, Collagen I, Collagen IV
α3	β1	Laminin-332, Laminin-511, Laminin-521, Collagen IV, Fibronectin
α5	β1	Fibronectin, Fibrinogen
α6	β1	Laminin-111, Laminin-211, Laminin-221, Laminin-332, Laminin-511, Laminin-521
	β4	Laminins-332, Laminin-511

α7	β1	Laminin-111, Laminin-211, Laminin-221
α8	β1	Fibronectin, Vitronectin
α10	β1	Collagen I, Collagen IV
αV	β1	Vitronectin, Fibronectin, Fibrinogen
	β5	Vitronectin
	β8	Vitronectin, Fibronectin, Collagen IV, Laminin-111

Activin A:

https://pubmed.ncbi.nlm.nih.gov/11069203

Schulte, K., Jonas, C., Krebs, R., & Röher, H. (2000). Activin A and activin receptors in the human thyroid: a link to the female predominance of Goiter? Hormone and Metabolic Research, 32(10), 390–400. https://doi.org/10.1055/s-2007-978660

https://www.sciencedirect.com/topics/medicine-and-dentistry/activin-a

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Retinoic acid:

https://pmc.ncbi.nlm.nih.gov/articles/PMC7764495

Szymański, Ł., Skopek, R., Palusińska, M., Schenk, T., Stengel, S., Lewicki, S., Kraj, L., Kamiński, P., & Zelent, A. (2020). Retinoic acid and its derivatives in skin. Cells, 9(12), 2660. https://doi.org/10.3390/cells9122660

https://pmc.ncbi.nlm.nih.gov/articles/PMC6791161/

Zasada, M., & Budzisz, E. (2019). Retinoids: active molecules influencing skin structure formation in cosmetic and dermatological treatments. Advances in Dermatology and Allergology, 36(4), 392–397. https://doi.org/10.5114/ada.2019.87443

WNT4:

https://www.ncbi.nlm.nih.gov/gene?Db=gene&Cmd=DetailsSearch&Term=54361

WNT4 Wnt family member 4 [Homo sapiens (human)] - Gene - NCBI. (n.d.).
https://www.ncbi.nlm.nih.gov/gene?Db=gene&Cmd=DetailsSearch&Term=54361
https://www.sciencedirect.com/topics/agricultural-and-biological-sciences/wnt4

Hepatocyte growth factor (HGF):

https://pmc.ncbi.nlm.nih.gov/articles/PMC3081175/

Nakamura, T., & Mizuno, S. (2010). The discovery of Hepatocyte Growth Factor (HGF) and its significance for cell biology, life sciences, and clinical medicine. Proceedings of the Japan Academy Series B, 86(6), 588–610. https://doi.org/10.2183/pjab.86.588

Transforming growth factor alpha (TGFA):

https://pmc.ncbi.nlm.nih.gov/articles/PMC4105142/

Singh, B., & Coffey, R. J. (2014). From wavy hair to naked proteins: The role of transforming growth factor alpha in health and disease. Seminars in Cell and Developmental Biology, 28, 12–21. https://doi.org/10.1016/j.semcdb.2014.03.003

Transforming growth factor beta (TGFB1):

https://www.ncbi.nlm.nih.gov/gene/7040#gene-expression

TGFB1 transforming growth factor beta 1 [Homo sapiens (human)] - Gene - NCBI. (n.d.).
https://www.ncbi.nlm.nih.gov/gene/7040#gene-expression

Insulin-like growth factor (IGF1):

https://pmc.ncbi.nlm.nih.gov/articles/PMC5488279/
Yakar, S., & Adamo, M. L. (2012). Insulin-Like growth Factor 1 physiology. Endocrinology and Metabolism Clinics of North America, 41(2), 231–247. https://doi.org/10.1016/j.ecl.2012.04.008

Platelet-derived growth factor (PDGFA):

https://pubmed.ncbi.nlm.nih.gov/15207811/
Fredriksson, L., Li, H., & Eriksson, U. (2004). The PDGF family: four gene products form five dimeric isoforms. Cytokine & Growth Factor Reviews, 15(4), 197–204. https://doi.org/10.1016/j.cytogfr.2004.03.007

Science buddies:

"Creating a Kidney: How Stem Cells Might Be Used to Bioengineer a Vital Organ." Science Buddies, 22 June 2023, https://www.sciencebuddies.org/science-fair-projects/project-ideas/BioMed_p013/medical-biotechnology/bioengineer-kidney-with-stem-cells. Accessed 15 Dec. 2025.
https://www.sciencebuddies.org/science-fair-projects/project-ideas/BioMed_p013/medical-biotechnology/bioengineer-kidney-with-stem-cells

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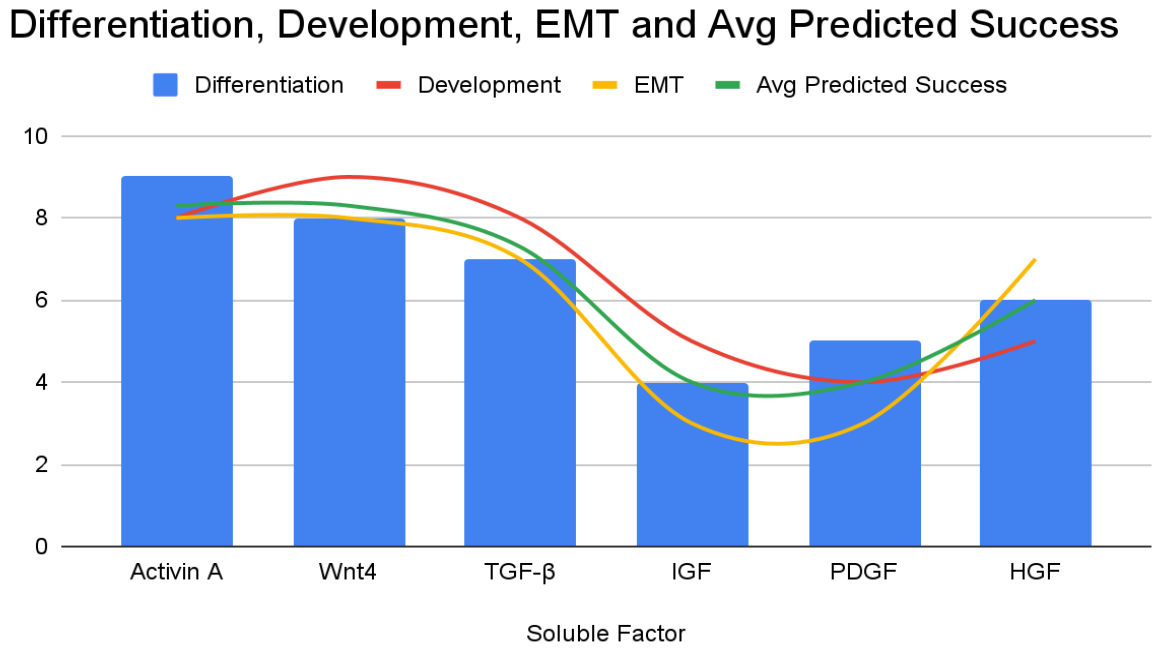
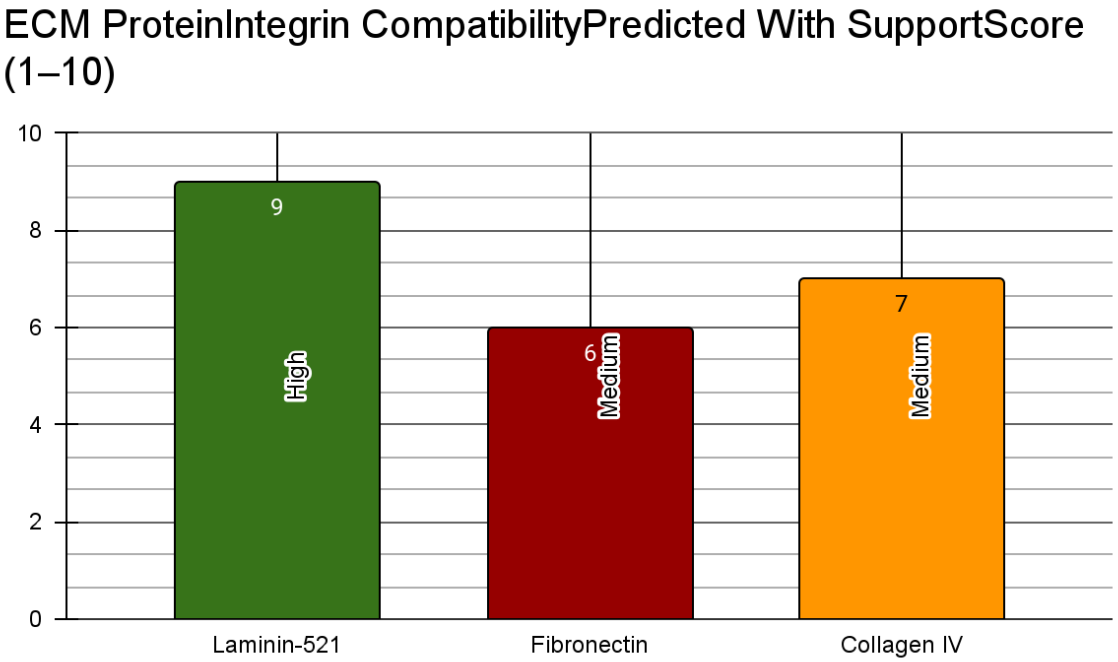
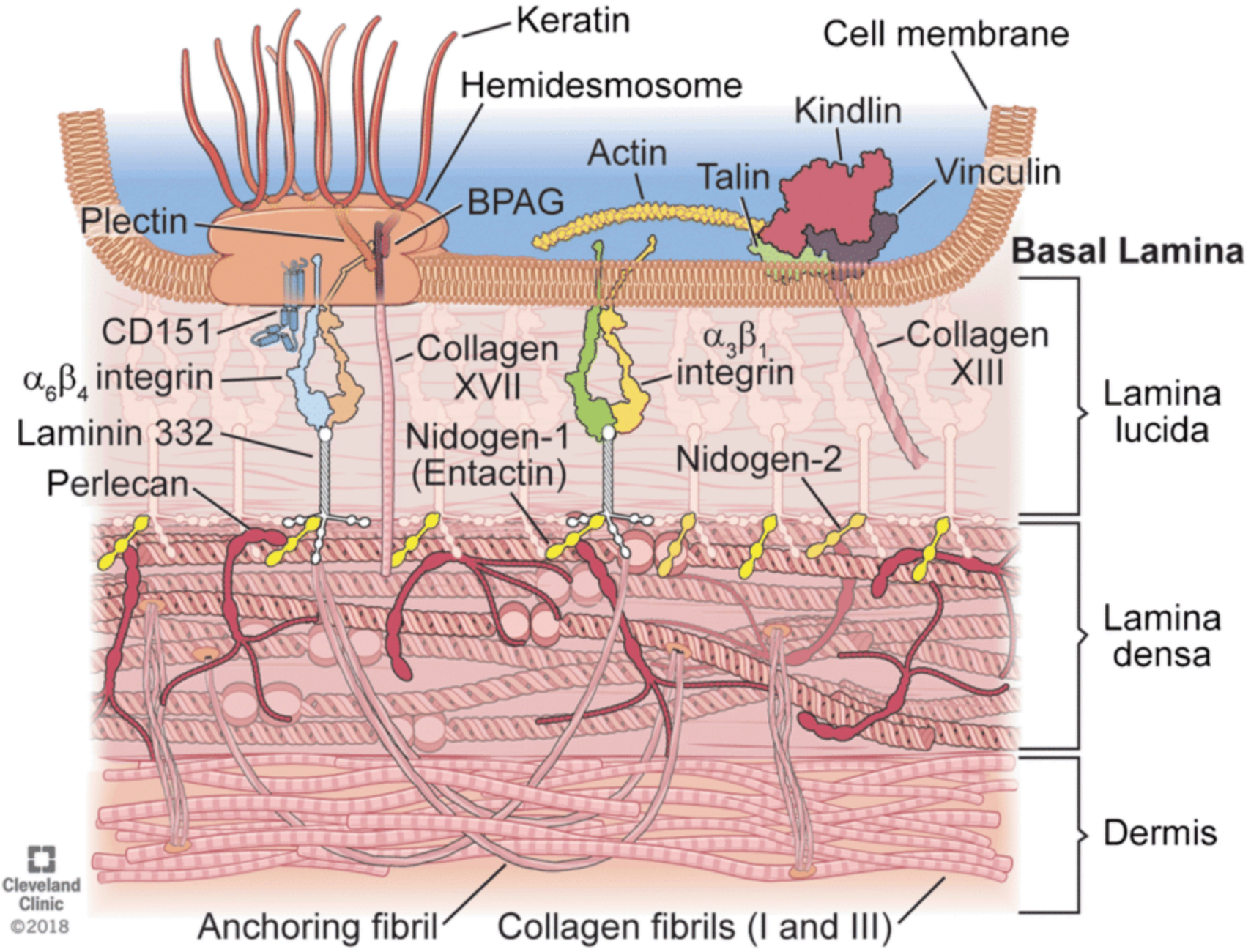


Soluble Factor	Differentiation	Development	EMT	Avg Predicted Success
Activin A	9	8	8	8.3
Wnt4	8	9	8	8.3
TGF-β	7	8	7	7.3
IGF	4	5	3	4
PDGF	5	4	3	4
HGF	6	5	7	6



ECM Protein	Integrin Compatibility	Predicted Support	Score (1–10)
Laminin-521	High	High	9
Fibronectin	Medium	Medium	6
Collagen IV	Medium	High	7

Trial	Factors	ECM	Avg Predicted Success
1	Activin A, Wnt4, TGF-β	Laminin-521	8.3 + 9 → 8.65
2	IGF, PDGF, HGF	Fibronectin	4.0 + 6 → 5.0
3	Activin A, Wnt4, HGF	Collagen IV	7.53 + 7 → 7.27


Keratin
Cell membrane
Hemidesmosome
Kindlin
Actin
Talin
Vinculin
BPAG
Plectin
Basal Lamina
CD151
Collagen XVII
$\alpha_3\beta_1$ integrin
Collagen XIII
$\alpha_6\beta_4$ integrin
Laminin 332
Nidogen-1 (Entactin)
Nidogen-2
Perlecan
Lamina lucida
Lamina densa
Dermis
Anchoring fibril
Collagen fibrils (I and III)
Cleveland Clinic ©2018

Closing:

Across all three trials, combinations that emphasized developmental signaling (Activin A, Wnt4, TGF-β) paired with laminin-based ECM proteins yielded the highest predicted nephron differentiation efficiency. Growth-focused conditions supported survival but showed lower differentiation specificity. Balanced environments combining developmental and EMT-regulating factors showed moderate predicted success, suggesting that precise pathway coordination is critical for nephron formation.

I hypothesized that testing different combinations of soluble signaling factors and ECM would yield distinct predicted levels of kidney cell differentiation, with combinations that share similar developmental roles and integrin interactions producing the strongest differentiation outcomes. My hypothesis was valid. This experiment used bioinformatics databases and published research to predict outcomes rather than performing live-cell culture experiments.

What I learned from this experiment was that a multitude of proteins and soluble factors can be used to help create new life for thoughts that do not have faith in what might happen to them in the future, and grow new horizons for thoughts that might need organ transplants, and how stem cells might be used to save the lives of billions.

Reflections:
How can bioinformatic databases be used to determine the best protein environment for bioengineering a kidney, and how can stem cells be used to bioengineer vital organs? That is the question I sought to answer, and I can say, with a truthful heart, that I know the answer. In this project, I explored successes in stem cell therapy and the most effective environments for growing stem cell kidneys.

This project was one of hardships and difficulties, but I still managed to have fun. The reason I speak of this so harshly is that it did not go smoothly. The reason is that I knew very little about this topic and had to teach myself. Also, the vocabulary for this project was exceedingly difficult. However, some of it did go well. For example, the amount of resources on all these topics was incommodious and, truthfully, partially inconvenient. The reason I say this is because there is so much information to absorb, and it is easily overwhelming. So the second you start trying, you are already exhausted and ready to be done.

Nevertheless, one of the redeeming factors is that once you are done, it is like you have finally fulfilled the purpose of life, you are at peace with the world, and you know you have something to brag about at the dinner table. If I did my project differently, I would learn a lot more about the topic and watch some videos to understand it better. The reality is, I was more successful in learning the topics; it was easier to learn all these concepts, and I spent most of my time teaching instead of working. Nevertheless, the important thing is that I had fun.

My Project's Importance to the World (real-world application):

Kidney disease affects millions of people worldwide, and many patients rely on kidney transplants to survive. However, there are not enough donor kidneys available, and patients who do receive transplants must take lifelong immunosuppressant medications, which can cause serious side effects and increase the risk of infection. Because of these challenges, there is a strong global need for new and improved treatments for kidney failure.

This project is important because it explores how patient-specific kidney cells can be generated from human induced pluripotent stem cells (hiPSCs). By studying how different soluble growth factors and extracellular matrix (ECM) proteins influence stem cell differentiation, this research helps scientists understand how to guide stem cells to differentiate into nephron cells, the functional units of the kidney. If successful, this approach could reduce the need for donor organs and lower the risk of immune rejection.

The methods used in this project also demonstrate how bioinformatics can be used to make scientific predictions without performing experiments on humans or animals. This saves time, reduces costs, and avoids ethical concerns while still producing meaningful scientific insights. The same approach could be applied to other organs, such as the liver or heart, expanding the impact of regenerative medicine.

Overall, this project contributes to the long-term goal of bioengineering functional organs for transplantation. Advances in this field could improve the quality of life, increase survival rates for patients with organ failure, and help address the global shortage of transplantable organs.