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REVIEW ARTICLE **OPEN ACCESS**

GATA 3: An Update

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ABSTRACT
Studies have shown that "before and after birth, the transcription element Gata3 is essential for the development of a wide range of tissues and cell lines". Researchers have also found that it is one of the main factors that determines the fate of cells and the shape of tissues. This is because it mostly works on stem and progenitor cells. Furthermore, studies have shown that "it controls the expression of important lineage-determining proteins as well as genes involved in the cell cycle, and it was also concluded that Gata3 participates in a number of stages of hematopoiesis in adults as well as throughout development". Thus, we conducted this review to know the basics of GATA3's role in the development of tissues and organs.
Key words: *GATA3, role, development, progenitor cell, tissue, gene.*

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INTRODUCTION

Studies have also concluded that hematopoiesis is the process of creating the cellular components that are necessary in order to make blood, and its name stems from the Greek phrase for "blood production." Research has also shown that these "components include red blood cells, white blood cells, platelets, and stem cells".[1] Researchers have also found that "all of these parts come from multipotent hematopoietic stem cells (HSCs), which are the main building blocks of this cell process". Furthermore, studies have shown that "HSCs also play the role of being the most important component in this cell process. The process of hemopoiesis is very intricate and convoluted, and it is controlled by a huge number of different signaling pathways and transcription factors. This process may be described as both complicated and very inventive. Studies have also concluded that the transcription factors work by themselves and are often organized into families with more than one gene".[2] Furthermore, studies have shown that "they are very important for turning on target genes for certain cell fates and turning off target genes for other cell fates at the same time. These different families of transcription factors are often found in cellular components one of which is GATA family. According to past studies, GATA family has total of 6 subgroups among which GATA 3 shares around 97% of its amino acid identity between both humans and mouse. Studies have also shown that GATA3 subgroup was found to be very important component or the development , maintainence , survival & proliferation of early T-cell progenitors, b cell, myeomonocytic & erythroid lineae".[2]

Researchers have also found that the B lymphoid program needs to be stopped in early lymphoid progenitors in order to help guarantee that these progenitors will develop into T cells.[3,4] This is due to the fact that Gata3 is necessary to foster and ensure the development of T cells. Furthermore, studies have shown that it plays the role of a master regulator of T helper type 2 cells within the T-cell lineage. Studies have further concluded that these cells are more often referred to as Th2 cells. Additionally, studies have found that these cells are responsible for orchestrating a wide range of immunological responses. Studies have also concluded that, because it can influence the genes that encode the Th2 cytokines Il4, Il5, and Il13, it is able to control the differentiation of Th2 cells.[5] Studies have also concluded that this allows it to govern the differentiation of Th2 cells. This is the means by which it achieves its objective. On the other hand, it would seem that the levels of Gata3 need to be carefully managed during the whole of the thymocyte formation process in order to guarantee the best possible outcomes. The failure of embryonic processes is caused by levels that are too low, while cytotoxicity is caused by levels that are too high.[6] In fact, studies have shown that "overexpressing Gata3 in the T-cell lineage stopped the maturation of the cytotoxic T-cell lineage and encouraged the growth of thymic lymphoblastoid tumors".[7] Studies have also shown that "overexpressing Gata3 in early fetal thymocyte stages also changed their lineage of

differentiation to become mast cells".[8] Studies have also found that the "T-cell lineage was responsible for both of these effects. The T-cell lineage was responsible for both of these effects, which were both seen".[1]
Various studies have shown that "GATA3 has also been implicated in T-cell acute lymphoblastic leukemia (T-ALL), which highlights the importance of this transcription factor in lymphoid development and function. Thus, in our review, we have tried to evaluate and discuss GATA3".[1]

ROLE IN DEVELOPMENT

Many studies have shown that "Gata3 is an important part of both figuring out what kind of cell it is and helping a wide range of cells, tissues, and organs grow in the early stages of development. Various studies have shown these examples, i.e., adipocytes [9], the kidney [10], the mammary gland [11], the skin [12,13], and the sympathetic nervous system (SNS)". [14,15,16] One study that looked at this topic looked at how Gata3 works in various systems. It found that because developing systems are close to each other in the embryo, Gata3's action in one tissue can affect the growth of a tissue next to it. This not only illustrates this occurrence but also gives vital insights into the molecular features of Gata3's activity.[17]

a. Skin & Hair

Studies have also concluded that the lineage of stem cells in the skin is determined by Gata3, which plays a crucial role in this process. Researchers have also found that this is expressed at the start of a process called the specification of inner root sheath (IRS) cells in hair follicles. Also, research has shown that when Gata3 was deleted by a LacZ knock-in, IRS progenitors couldn't change into IRS and make IRS, which led to the development of an abnormal hair structure.[13] In addition to this, studies have also concluded that this was due to the fact that IRS progenitors were unable to go through the differentiation process. In addition, as compared to the other members of the GATA family, the interfollicular epidermis displays the greatest level of expression for the gene gata3. Also, studies have found that when Gata3 was removed from the top layer of skin using a mouse line that expresses a protein called keratin-14-Cre (K14-Cre), the skin lost its ability to selectively block certain substances. This led to the death of the fetus. The mice had irregularities in the differentiation of their skin, a disturbed layout of their hair follicles, and a delay in the growth and maintenance of their hair. Studies have concluded that the mice were subjected to a genetic study, which revealed that there was an error in the manufacturing of lipids. There is a possibility that this is due to the deletion of the gene encoding lipid acetyltransferase (Agpat5), which is directly controlled by Gata3.[12,18] Previous research has shown that Gata3 is connected to adipogenesis and that the gene stops adipocytes from differentiating.[9]

b. Kidney

A study also found that "GATA3, also called Gata3, is the only GATA factor that is expressed in the urogenital system before embryonic day 12.5 (E12.5). It is essential to have the nephric duct present in order for it to function in the appropriate manner. In order to avoid ectopic metanephric kidney system development and early nephric duct differentiation, Grote et al., selectively deleted Gata3 from the nephric duct system, which resulted in significant defects in the urogenital system".[19,20] Renal dysplasia has also resulted from Gata3 haploinsufficiency, according to the findings of the research. Studies have also concluded that Gata3 has also been linked to clear-cell renal cell carcinoma, which is the kind of renal cell carcinoma that affects the majority of patients. cc-RCC stands for clear cell renal cell carcinoma. Cooper et al., demonstrated that when promoter hypermethylation downregulated Gata3 expression, Type III TGF-b receptor (TbRIII), a betaglycan protein with the capacity to control tumor growth, had lower expression.[21]

c. Inner Ear

A study also found that throughout the process of developing the ear, Gata3 is widely expressed in a variety of cell types.[22,23,24] Studies have also concluded that these cell types include the supportive cells, the inner hair cells, and the outside hair cells. According to additional research, mice that are heterozygous for the Gata3 gene experience significant damage throughout the cochlea of the inner ear, which results in hearing loss.[25] Furthermore, studies have also concluded that this degradation may be seen throughout the whole inner ear. Studies have also concluded that the cochlea deteriorates in a manner that results in hearing loss as a result of this degeneration, which occurs. Several other studies have also found this to be true in people with HDR syndrome who only have one functional copy of GATA3 and who also have low parathyroid levels, hearing loss, and problems with their kidneys.[26,27]. Studies have also concluded that this symptom is comparable to what is seen in individuals who suffer from HDR syndrome. In addition to this, studies have also concluded that individuals with HDR syndrome only have one functional copy of the GATA3 gene.[1]

d. Mammary Gland(MG)

A study also found that during embryogenesis, the creation of the MG requires Gata3, which is essential for this process. Other studies have also concluded that,here the transcription factor that has the greatest expression is shown by genome-wide transcript analysis.[28] It was also discovered that the MG couldn't make terminal end buds (TEBs) because Gata3 was taken out of the epithelium using the MMTVCre gene at the start of puberty.[29,28] Studies have further concluded that this may preventes the MG from developing. Studies have also found that the fact that mutations in this gene are linked to about 10% of all human breast cancers is more proof that the GATA3 gene is very important for MG. Furthermore, studies have also shown that the C-terminal second zinc finger is the location where the vast majority of somatic mutations are found.[30] Furthermore, studies have proved that despite the fact that there are a wide variety of somatic mutations, this is still the case. Studies that have been carried out both in vitro and in vivo have revealed evidence that suggests the role of GATA3 as a tumor suppressor gene. This evidence has shown that there is evidence that indicates the role of GATA3 as a tumor suppressor gene. Also, research has shown that when Gata3 was lost, breast cancer started to grow and spread in a model of a luminal tumor in mice.[31] Certain genes, like ID1, ID3, KRTHB1, LY6E, and RARRES3, can be turned off when the GATA3 gene is expressed. These genes are linked to metastasis. This, in turn, can inhibit the progression of breast cancer and pulmonary metastasis.[32] Also, research found that restoring the expression of the Gata3 gene in a mouse model of breast cancer differentiation caused the breast cancer to differentiate and stopped it from spreading.[31] A study also discovered that increasing the expression of the GATA3 gene can lower the spread of breast cancer by blocking the activity of genes related to metastasis, such as ID1, ID3, KRTHB1, LY6E, and RARRES3.[33] It was also discovered that restoring Gata3 gene expression in a mouse model of breast duct differentiation started breast cancer duct differentiation and stopped it from spreading. Besides this, it has been shown that GATA3 raises the level of microRNA-29b (miR-29b), which either helps or hurts differentiation and changes the environment around the tumor.[34] In addition, studies have also concluded that reduced GATA3 expression is associated with a poorer prognosis for breast cancer patients as well as a more aggressive illness. On the other hand, studies have shown that breast cancer patients who expressed GATA3 had a better outlook, a lower risk of recurrence, and a higher overall survival rate.[35] A study found that GATA3 may not play a clear role in breast cancer because it was found to help make estrogen-responsive tumors by directly connecting to and turning on the estrogen receptor a (ERa) tumor gene.[36] This is due to the fact that it was found out in another study that GATA3 plays a role in breast cancer. Studies have also concluded that GATA3 gene expression in breast cancer tumors is associated with a better prognosis.[37, 38 39] This may be one of the reasons why ERa-positive tumors have a more differentiated phenotype and are often less aggressive than other types of breast cancer.[1]

e. Sympathetic Nervous System

It has also been discovered through various studies in their investigations that, in the growth of the SNS, Gata3 plays an essential role.[40,41,42,43,44] In fact, studies have also concluded that this is the reason why a deletion of the Gata3 gene at around E11.5 in the developmental timeline is embryonically lethal. It was possible to pharmacologically rescue the mice by feeding the mothers DOPS, a synthetic catecholamine intermediate.[40] Studies have further concluded that this mortality was associated with a deficiency of noradrenaline in the SNS, and it was able to do so. Also, studies found that it was possible to find a link between this death rate and a lack of noradrenaline in the SNS. Furthermore, research has shown that the production of tyrosine hydroxylase, an enzyme needed for duct synthesis, is also necessary for the production of catecholamines, which are SNS mediators. Additionally, it plays a significant role in the survival of sympathetic neurons, both in adults and in embryos.[41,42]

CONCLUSION

Gata3 is needed for the growth of many types of cells, organs, and tissues. If it is disrupted during development, it causes serious problems in those systems, which eventually kill the embryo in the middle of pregnancy after the germline is deleted. We looked at the effects of deleting Gata3 in a lot of different systems and found that Gata3 is mostly expressed in the stem and progenitor cells, which control how cells differentiate and decide what fate to take. This was discovered as a result of the analysis of the phenotypes of the Gata3 deletion. It seems to stop kidney cells from differentiating too soon and preadipocytes from differentiating, but it seems to help skin cells and mammary gland cells differentiate. However, in the grand scheme of things, its function is to guarantee accurate tissue development.

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