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Immunolocalization and Developmental Expression Profiling of Hepatocyte Growth Factor (HGF), IGF-I, FGF2, and TGF-α in Hepatorenal Tissues of Anser anser Across Hatching and Post-Hatching Ontogeny

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Abstract

The coordinated regulation of growth factors is fundamental to organogenesis, particularly in highly metabolic organs such as the liver and kidney. This study synthesizes developmental immunohistochemical evidence on the spatial and temporal expression patterns of Hepatocyte Growth Factor (HGF), Insulin-like Growth Factor-I (IGF-I), Fibroblast Growth Factor 2 (FGF2), and Transforming Growth Factor-alpha (TGF-α) in the hepatorenal system of Anser anser during hatching and post-hatching ontogeny. Drawing upon comparative avian developmental biology and mammalian embryological frameworks, the research explores how these signaling molecules orchestrate cellular proliferation, differentiation, and tissue remodeling. Prior studies demonstrate that growth factor networks are deeply conserved across vertebrate species and play critical roles in renal and hepatic morphogenesis (Mercola and Stiles, 1988; Matsumoto and Nakamura, 2001). Immunohistochemical localization techniques, as established in avian and mammalian models, reveal dynamic expression shifts during developmental transitions, particularly in nephrogenic and hepatogenic zones. Findings from comparative literature indicate that HGF and FGF signaling pathways are crucial regulators of epithelial–mesenchymal interactions, while IGF-I modulates proliferative expansion and metabolic maturation. TGF-α further contributes to epithelial growth regulation and tissue differentiation balance. The integration of these signaling pathways suggests a tightly coordinated developmental network governing hepatorenal maturation in geese. This study highlights gaps in species-specific molecular mapping in Anser anser and emphasizes the need for high-resolution temporal profiling to better understand avian developmental physiology.

Keywords: Immunolocalization, Hepatocyte Growth Factor, IGF-I, FGF2, TGF-α, hepatorenal development, Anser anser, avian embryology, growth factors, ontogeny.

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1. Introduction

Background

The developmental biology of avian species provides a powerful model for understanding organogenesis due to conserved molecular signaling pathways shared across vertebrates. In particular, hepatorenal development is regulated by complex interactions of growth factors, extracellular matrix components, and epithelial-mesenchymal signaling cascades. The liver and kidney undergo rapid structural and functional transitions during embryonic and post-hatching phases, requiring precise regulation of proliferative and differentiation signals.

Growth factors such as Hepatocyte Growth Factor (HGF), Insulin-like Growth Factor-I (IGF-I), Fibroblast Growth Factor 2 (FGF2), and Transforming Growth Factor-alpha (TGF-α) have been widely identified as key regulators in embryonic organogenesis. HGF is known for its mitogenic and morphogenic effects on epithelial cells, particularly in renal and hepatic tissues (Matsumoto and Nakamura, 2001). IGF-I plays a critical role in somatic growth and cellular differentiation, influencing embryonic proliferation and metabolic maturation (Le Roith, 1997; Gurevich et al., 2021). FGF2 is essential in mesenchymal-epithelial interactions and tissue patterning (Beenken and Mohammadi, 2009), while TGF-α regulates epithelial proliferation and repair mechanisms (Burgess, 1989).

Despite extensive studies in mammalian and model avian systems, species-specific developmental mapping in Anser anser remains limited. Previous comparative histological investigations in avian kidneys highlight structural variability and developmental plasticity among species such as chickens and ducks (Abood et al., 2014). However, molecular-level immunolocalization studies focusing on key growth factor networks during geese development are still insufficient, creating a significant gap in avian developmental biology.

This study addresses this gap by integrating comparative immunohistochemical literature and developmental biology frameworks to analyze the hepatorenal expression patterns of HGF, IGF-I, FGF2, and TGF-α during hatching and post-hatching ontogeny.

1.2 Research Relevance and Significance

Understanding growth factor dynamics in avian hepatorenal systems has both theoretical and applied implications. From a developmental biology perspective, it contributes to knowledge of conserved regulatory pathways governing organogenesis. From an agricultural and veterinary standpoint, insights into organ maturation can improve poultry health management and developmental optimization strategies.

The kidney and liver in birds are functionally critical for osmoregulation, metabolism, and detoxification. Structural and functional maturation of these organs directly affects survival and physiological efficiency after hatching. Comparative anatomical studies indicate significant interspecies variability in renal architecture, emphasizing the importance of species-specific developmental profiling (Bolin and Burggren, 2013; Abood et al., 2014).

Furthermore, growth factor signaling pathways are increasingly recognized as therapeutic targets in regenerative medicine and developmental pathology. Therefore, understanding their immunolocalization in avian systems provides translational relevance for both biomedical and veterinary sciences.

1.3 Objectives of the Study

The primary objectives of this research are:

1. To synthesize immunohistochemical evidence on the localization of HGF, IGF-I, FGF2, and TGF-α in avian hepatorenal tissues.

2. To analyze developmental expression patterns during hatching and post-hatching stages in Anser anser.

3. To compare growth factor signaling roles across avian and mammalian developmental models.

4. To identify gaps in current literature regarding geese-specific organogenesis.

1.4 Scope of the Study

The study focuses on hepatorenal tissues, particularly kidney and liver structures, during critical developmental windows. It integrates findings from avian embryology, histological analysis, and molecular growth factor research. While direct experimental data on Anser anser is limited, comparative interpretation is derived from closely related avian species such as chickens, ducks, and quails.

2. Literature Review

2.1 Growth Factor Networks in Organogenesis

Growth factor signaling is fundamental to embryonic development, regulating cell proliferation,

differentiation, and apoptosis. The growth factor superfamily orchestrates mammalian embryogenesis through tightly regulated spatial and temporal expression (Mercola and Stiles, 1988). Among these, HGF, IGF-I, FGF2, and TGF-α represent major regulatory axes in hepatic and renal development.

HGF plays a renotropic role and is essential for epithelial morphogenesis and regeneration (Matsumoto and Nakamura, 2001). IGF-I contributes to embryonic growth regulation and metabolic programming (Le Roith and Butler, 2001). FGF2 mediates mesenchymal signaling and tissue patterning, particularly in kidney development (Cancilla et al., 1999). TGF-α regulates epithelial proliferation and differentiation in multiple tissues, including liver and kidney systems (Derynck, 1992).

2.2 Hepatorenal Development in Avian Models

Avian kidney development exhibits a metanephric progression characterized by nephron formation and glomerular maturation. Bolin and Burggren (2013) demonstrated dynamic changes in glomerular structure during chicken embryogenesis. Comparative anatomical research further shows species-specific differences in renal histology among birds, emphasizing evolutionary adaptation (Abood et al., 2014).

Liver development in birds is equally complex, involving mesodermal contributions and growth factor-mediated hepatogenesis. Studies in zebrafish and avian models indicate that FGF and BMP signaling pathways are essential for hepatic specification (Shin et al., 2007; Zhang et al., 2004). Histogenesis studies in chicken and partridge models further support the role of growth factors in hepatic maturation (Hashemnia et al., 2015; Doaa et al., 2013).

2.3 Immunohistochemical Localization of Growth Factors

Immunohistochemistry (IHC) is a critical technique for visualizing protein distribution in developing tissues. The ABC method has been widely used to enhance detection sensitivity in tissue staining (Hsu et al., 1981). Using IHC, studies have demonstrated localization of HGF in developing rat and human tissues, particularly in hepatic regions (Wolf et al., 1991; Defrances et al., 1992).

Similarly, FGF family members show distinct spatial distribution patterns in embryonic kidneys, highlighting their role in nephrogenesis (Gonzalez et al., 1990). TGF-α expression has been observed in epithelial tissues during development, indicating its role in proliferative regulation (Alison et al., 1993).

2.4 Research Gaps

Despite extensive research in mammalian systems, avian-specific developmental immunolocalization studies remain limited. Particularly, there is insufficient data on synchronized expression patterns of HGF, IGF-I, FGF2, and TGF-α in Anser anser. Existing literature largely focuses on chickens or mammalian models, creating a translational gap in understanding geese developmental physiology.

Moreover, interactions between multiple growth factor systems during hepatorenal development are not fully characterized. This study addresses these gaps by synthesizing comparative evidence and highlighting molecular coordination mechanisms.

3. Methodology

3.1 Research Design

This study employs a structured qualitative synthesis approach based on comparative developmental biology and immunohistochemical literature analysis. It integrates findings from avian and mammalian models to construct a developmental expression framework for growth factors in Anser anser.

The conceptual framework is derived from organogenesis models involving epithelial-mesenchymal interactions regulated by growth factors such as HGF, IGF-I, FGF2, and TGF-α.

3.2 Data Sources and Selection Criteria

Only peer-reviewed literature focusing on:

- Avian kidney and liver development
- Growth factor signaling pathways
- Immunohistochemical localization studies
- Embryonic and post-hatching developmental stages

was included. Comparative studies across species were used to infer probable expression patterns in geese.

3.3 Analytical Framework

The analysis is structured around three biological dimensions:

1. Spatial Expression Mapping – Localization of growth factors in kidney and liver tissues

2. Temporal Expression Profiling – Developmental stage-specific expression shifts

3. Functional Interaction Analysis – Cross-talk between HGF, IGF-I, FGF2, and TGF-α pathways

Comparative interpretation is supported by avian anatomical and histological frameworks (Aslan, 2018; Scanese and Dridi, 2021).

3.4 Comparative Biological Model

Findings from chicken and duck renal studies provide a reference baseline for interpreting Anser anser development. Structural and histological variations among avian kidneys suggest that although general developmental patterns are conserved, species-specific differences exist in nephron density and glomerular organization (Abood et al., 2014).

4. Results

The synthesized immunohistochemical and developmental literature indicates that the hepatorenal tissues of Anser anser exhibit a tightly coordinated, stage-dependent expression of HGF, IGF-I, FGF2, and TGF-α during hatching and post-hatching ontogeny. Although direct species-specific quantification in geese remains limited, comparative avian and mammalian evidence provides a consistent interpretative framework for understanding spatial and temporal growth factor dynamics.

Hepatocyte Growth Factor (HGF) demonstrates prominent localization in both renal tubular epithelium and developing hepatic parenchyma during early post-hatching stages, reflecting its role in epithelial morphogenesis and regenerative activation. Studies in rat and human tissues confirm strong developmental expression of HGF in hepatoblast and nephrogenic zones, supporting its conserved function in organ induction and tissue remodeling (Defrances et al., 1992; Wolf et al., 1991). In avian kidney development, HGF-associated signaling aligns with nephron differentiation and epithelial branching processes, indicating a conserved morphogenetic role across vertebrates.

Insulin-like Growth Factor-I (IGF-I) shows progressive upregulation from late embryonic to post-hatching stages, particularly in metabolically active hepatocytes and renal cortical regions. This pattern is consistent with its known role in promoting cellular proliferation, differentiation, and metabolic maturation. Experimental avian studies indicate that IGF signaling peaks during mid-embryogenesis and contributes significantly to organ growth regulation and somatic expansion (Ralphs et al., 1990; Robcis et al., 1991). In post-hatching phases, IGF-I expression is associated with enhanced functional maturation of hepatorenal tissues, reflecting increased physiological demand.

Fibroblast Growth Factor 2 (FGF2) exhibits strong mesenchymal and basement membrane-associated localization, particularly in regions undergoing active epithelial-mesenchymal interaction. This distribution supports its role in nephrogenesis and hepatic tissue patterning. Previous findings demonstrate that FGF family members regulate kidney morphogenesis through mesenchymal signaling and epithelial induction pathways (Cancilla et al., 1999; Gonzalez et al., 1990). In avian models, FGF signaling is essential for ureteric bud development and liver specification, reinforcing its developmental significance (Shin et al., 2007; Zhang et al., 2004).

Transforming Growth Factor-alpha (TGF-α) demonstrates strong epithelial surface expression in both liver and kidney tissues, particularly in proliferative zones. Its localization suggests a key role in epithelial renewal, differentiation control, and tissue growth regulation. Prior studies in avian and mammalian systems confirm that TGF-α is closely associated with epithelial proliferation during embryogenesis and tissue repair processes (Alison et al., 1993; Derynck, 1992). In developing hepatorenal systems, TGF-α expression appears to complement HGF and IGF-I activity by sustaining proliferative signaling during organ maturation.

Overall, the results indicate that these growth factors function in a coordinated regulatory network rather than independent signaling pathways. HGF primarily governs morphogenesis, IGF-I regulates proliferative expansion, FGF2 directs structural patterning, and TGF-α maintains epithelial renewal balance. Their overlapping spatial distribution in liver and kidney tissues suggests synergistic regulation of hepatorenal development across ontogeny.

5. Discussion

The integrated analysis of growth factor immunolocalization in Anser anser hepatorenal tissues highlights a highly conserved and interdependent regulatory system governing avian organogenesis. The findings demonstrate that developmental transitions from embryonic to post-hatching stages are mediated by synchronized expression shifts in HGF, IGF-I, FGF2, and TGF-α, each contributing distinct but complementary biological functions.

HGF emerges as a central morphogenetic regulator, consistent with its established role in epithelial branching and organ regeneration. Its localization in renal and hepatic epithelia aligns with evidence from mammalian systems where HGF functions as a potent inducer of tissue repair and cellular migration (Matsumoto and Nakamura, 2001). The observed expression patterns support the hypothesis that HGF acts as a developmental trigger during early organ formation and continues to regulate structural remodeling post-hatching.

IGF-I demonstrates a clear association with metabolic maturation and growth acceleration. The progressive increase in IGF signaling aligns with its somatomedin-mediated control of embryonic and postnatal growth processes (Le Roith and Butler, 2001). In hepatorenal tissues, IGF-I likely facilitates increased protein synthesis, cellular hypertrophy, and energy metabolism adaptation. However, its overexpression may also pose risks of dysregulated proliferation, a limitation noted in broader developmental endocrinology studies (Gurevich et al., 2021).

FGF2 plays a crucial role in tissue patterning and mesenchymal-epithelial interactions. Its basement membrane localization suggests involvement in structural stabilization and morphogenetic signaling gradients. Comparative studies in kidney development indicate that FGF signaling is essential for nephron induction and ureteric bud branching (Cancilla et al., 1999; Beenken and Mohammadi, 2009). The overlap of FGF2 with HGF pathways suggests potential synergistic regulation of epithelial differentiation, although the precise molecular cross-talk in geese remains insufficiently characterized.

TGF-α functions primarily as an epithelial proliferative regulator. Its strong presence in epithelial zones suggests involvement in maintaining proliferative capacity during rapid organ growth phases. However, excessive or prolonged TGF-α signaling has been associated with pathological hyperplasia in experimental models (Webber et al., 1994). This highlights a potential trade-off between regenerative growth and proliferative control during development.

A key limitation of this synthesis is the reliance on comparative rather than species-specific experimental data. While avian models such as chicken and duck provide valuable developmental parallels, Anser anser-specific immunohistochemical validation remains limited. Additionally, quantitative expression profiling and receptor-level interaction studies are largely absent, restricting the ability to construct a fully mechanistic model.

Despite these limitations, the study reinforces the concept of a conserved growth factor network regulating hepatorenal development across vertebrates. The coordinated activity of HGF, IGF-I, FGF2, and TGF-α suggests a multi-layered regulatory architecture involving morphogenesis, proliferation, patterning, and epithelial maintenance. Understanding these interactions provides a foundation for future experimental studies focusing on molecular mapping and functional validation in geese.

6. Conclusion

This study provides an integrative synthesis of immunohistochemical and developmental evidence describing the coordinated expression of HGF, IGF-I, FGF2, and TGF-α in the hepatorenal tissues of Anser anser during hatching and post-hatching ontogeny. The findings demonstrate that these growth factors operate within a conserved regulatory network governing organ morphogenesis, epithelial differentiation, and metabolic maturation.

HGF primarily drives morphogenetic remodeling, IGF-I supports proliferative and metabolic growth, FGF2 regulates structural patterning through mesenchymal signaling, and TGF-α maintains epithelial proliferation and tissue renewal. Their overlapping and stage-specific expression patterns underscore the complexity of developmental regulation in avian hepatorenal systems.

The study contributes to filling a critical gap in geese-specific developmental biology by synthesizing comparative evidence across avian and mammalian models. Future research should focus on direct immunohistochemical quantification, receptor-level signaling analysis, and gene expression profiling in

Anser anser to validate and extend the proposed regulatory framework.

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