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Chicken Embryo Model Perspective : Novel and Relevant Models Immunity-Based Research: A Systematic Review

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Abstract, *Dysregulation of the immune system is associated with many medical conditions, including: Cardiovascular disease, diabetes, cancer. Most popular model today. In biomedical research, rodents, despite the many advantages they offer, there are also many drawbacks to its use. Recently, another in vivo model, the chicken Embryos and their chorioallantoic membranes are resurfaced for a variety of uses. This model includes cost-effectiveness, time-efficiency, Easier to use. This review describes how to use chicken embryos. As a model for immune-based research because it gradually develops the embryonic immune system, Systems functionally similar to humans. This study examined mainly intended to describbe the immune system of birds, highlighting the differences and similarities with the human immune system A system containing a repertoire of lymphoid tissue, immune cells, and other important functions. A literature search was carried out systematically through the PubMed, NCBI, Google Scholar databases using keywords, namely, "Chicken embryo model, Perspective, Novel and relevant models Immunity, based research". Based on these keywords, 21350 articles were obtained and 50 articles that meet the inclusion and exclusion criteria were selected. Those helped to describe general in-ovo immune ontogeny. Future studies are suggested to better tailor the use of chicken embryo models for testing carrying out specific experimental hypotheses or preclinical studies.*

Keywords: *Chicken Embryo Model, Embryonic Immune System, Immunity, Novel Relevant Models, Research Based.*

1. BACKGROUND

Protection and equilibrium maintenance are two of the immune system's primary roles. how effective Skin protection relies on the fine balance between activation and tolerance. It protects the body against threats like infections and aberrant cells by avoiding interfering with its own cells. Sadly, this equilibrium isn't always rock solid; in fact, it can fall apart entirely in instances of diseases affecting the immune system. Here we are dealing with a broad variety of diseases: Cancer and diabetes, which show themselves more subtly, are not among them, nor are immunodeficiency and autoimmune diseases. Heart conditions. There is an urgent need for remedies to aid those affected by these ailments due to their prevalence. Consequently, at this stage However, immunology research needs to better understand the signaling pathways involved in order to create new treatments (Achkar et al., 2020; Carbone, 2021; Cox et al., 2015; Dünker, 2019; El-Gabalawy et al., 2010; Furman et al., 2019; H et al., 2016; Kundeková et al., 2021; Marcion et al., 2021; Mestas & Hughes, 2004; Noh et al., 2014; Nowak-Sliwinska et al., 2014; O'Connor et al., 2009; Ribatti, 2016; Schneider-Stock et al., 2020).

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The immune system is a complex network of interrelated proteins that consists of many cells, cytokines, chemokines, and other interacting proteins; it is not completely reproducible in vitro. Most Commonly Used Animals in Modern Biomedicine Subjects in the research are rodents. Being a mammal means its biology is studied extensively, and its immune system is similar to ours. It doesn't matter how helpful rat models are; they can never be totally accurate. Testing on living beings is the most glaring ethical dilemma. The estimated number of rats used for this purpose exceeds 100 million. The US is the only country that does experiments annually. It is possible for animals to experience pain during many biological research. Immune system related experiments. I am quite irritated by it. Potentially having a major effect on animal health is the rat immune system. One typical modulator that has the potential to induce inflammation is injectable lipopolysaccharide, or LPS. Your mouse may experience some unforeseen modifications as a result of this. Mental health issues and unpleasant emotions recognized. In addition to the clear moral dilemmas, there are major roadblocks caused by the immune system difference between rats and humans. While rats have shown promise as an animal model for several biological studies, they are by no means the exclusive option. The first part (Boehm et al., 2012; J. B. Murphy, 1913; Rezzola et al., 2020; Ribatti & Tamma, 2019; Rous & Murphy, 1911).

The growing importance of in vivo models Importantly, the Chorioallantoic Membrane (CAM) is used in the chicken embryo model. In fact, Vogel CAM facilitates gas exchange by providing an extensive capillary network to the egg, much as it does in the placentas of mammals. Using it won't cause any trouble. Biomedical study for a variety of purposes, including tumor development, therapeutic response, assessment of angiogenesis, and metastasis. There is nothing really novel about this model. It was first shown in 1911 by Rous and Murphy. Development of CAM-implanted chicken sarcoma tumors (Boehm & Swann, 2014; Davison, 2014; Franchini & Ottaviani, 2017; Ifrah et al., 2017; Kaiser & Balic, 2015; Oláh et al., 2014; Thapa & Farber, 2019; Yu & Scadden, 2016). Since then, it has been characterized and explored at length. It is now well known (Brand et al., 1983; Buettner & Bode, 2011; Glick, 1994; Madej et al., 2013; Siatskas & Boyd, 2000; Stebegg et al., 2018). Here, we take a look at Mostly intended for use in bird descriptions Analyzing the immune system, drawing attention to its parallels and contrasts with the human immune system A complex network that includes lymphoid tissues, immunological cells, and several other vital components.

2. THEORETICAL STUDY

The immune system is theoretically defined as a regulatory biological network responsible for maintaining host integrity through coordinated defensive and tolerance mechanisms. Immune homeostasis emerges from the dynamic balance between immune activation, which eliminates pathogens and abnormal cells, and immune tolerance, which prevents excessive responses toward self-antigens. At barrier interfaces such as the skin, this balance is particularly critical, as immune cells are continuously exposed to environmental stimuli while simultaneously maintaining tissue integrity. Disruption of immune homeostasis results in maladaptive immune responses, which may manifest as chronic inflammation or immune-mediated tissue damage(Davison, 2014; Ifrah et al., 2017; Oláh et al., 2014).

From a systems immunology perspective, immune function arises from multiscale interactions among immune cells, soluble mediators such as cytokines and chemokines, and intracellular signaling pathways. These components form nonlinear regulatory circuits that are highly context-dependent and sensitive to perturbations. Consequently, immune responses cannot be fully replicated in isolated in vitro systems, as such models fail to capture cellular crosstalk, spatial organization, and vascular interactions that are essential for immune regulation(Boehm et al., 2012; Boehm & Swann, 2014).

To address this complexity, in vivo models have been traditionally employed to study immune mechanisms. Rodent models are widely used due to their evolutionary proximity to humans and the extensive characterization of their immune systems. However, theoretical limitations arise from interspecies differences in immune architecture, signaling dynamics, and inflammatory thresholds. For example, systemic immune activation induced by agents such as lipopolysaccharide (LPS) can trigger exaggerated or non-physiological inflammatory responses in rodents, thereby confounding the interpretation of immune modulation and homeostatic regulation. These discrepancies highlight the conceptual gap between rodent immune responses and human immunopathology.

Within the theoretical framework of comparative immunology, alternative in vivo models provide complementary insights into conserved immune mechanisms while minimizing species-specific artifacts. The chicken embryo chorioallantoic membrane (CAM) represents a vascularized, extraembryonic system that supports gas exchange and tissue growth, analogous in function to the mammalian placental interface. The CAM provides a biologically integrated environment in which immune-related processes such as inflammation, angiogenesis, and tissue remodeling can be observed in vivo without the confounding influence of a fully mature adaptive immune system (Kundeková et al., 2021; Ribatti, 2016).

The avian immune system exhibits both conserved and divergent features relative to mammalian immunity. While birds possess unique lymphoid structures, including the bursa of Fabricius, the fundamental principles of innate immune recognition, cytokine-mediated signaling, and leukocyte recruitment are evolutionarily conserved. In the chicken embryo, innate immune mechanisms dominate early developmental stages, offering a simplified yet physiologically relevant system to study immune activation and vascular–immune interactions. This theoretical simplicity allows clearer interpretation of cause–effect relationships within immune signaling networks (Glick, 1994; Ifrah et al., 2017; Madej et al., 2013).

Thus, from a theoretical standpoint, the CAM model can be conceptualized as an intermediate in vivo platform that bridges the gap between reductionist in vitro systems and complex mammalian models. Its utility lies in enabling the investigation of immune-associated processes within a controlled, vascularized, and ethically less problematic biological context, making it particularly relevant for studies focused on immune regulation, inflammation, and tissue–immune interactions.

3. RESEARCH METHODS

A comprehensive literature search was carried out using the following keywords: "Chicken embryo model, Perspective, Novel and relevant models Immunity based research" in the PubMed, NCBI, and Google Scholar databases. Starting with terms like "Chicken embryo model, Perspective, Novel and relevant models Immunity,based research" and "journals that didn't charge for the articles," we were able to refine our search to include just publications that fulfilled our inclusion criteria. Articles are reviewed for data if they meet the inclusion criteria; otherwise, they are eliminated. Articles are reviewed for data if they meet the inclusion criteria; otherwise, they are eliminated, as shown on **Table 1** and **Figure 1.** This systematic review was conducted and reported in accordance with the PRISMA 2020 guidelines.

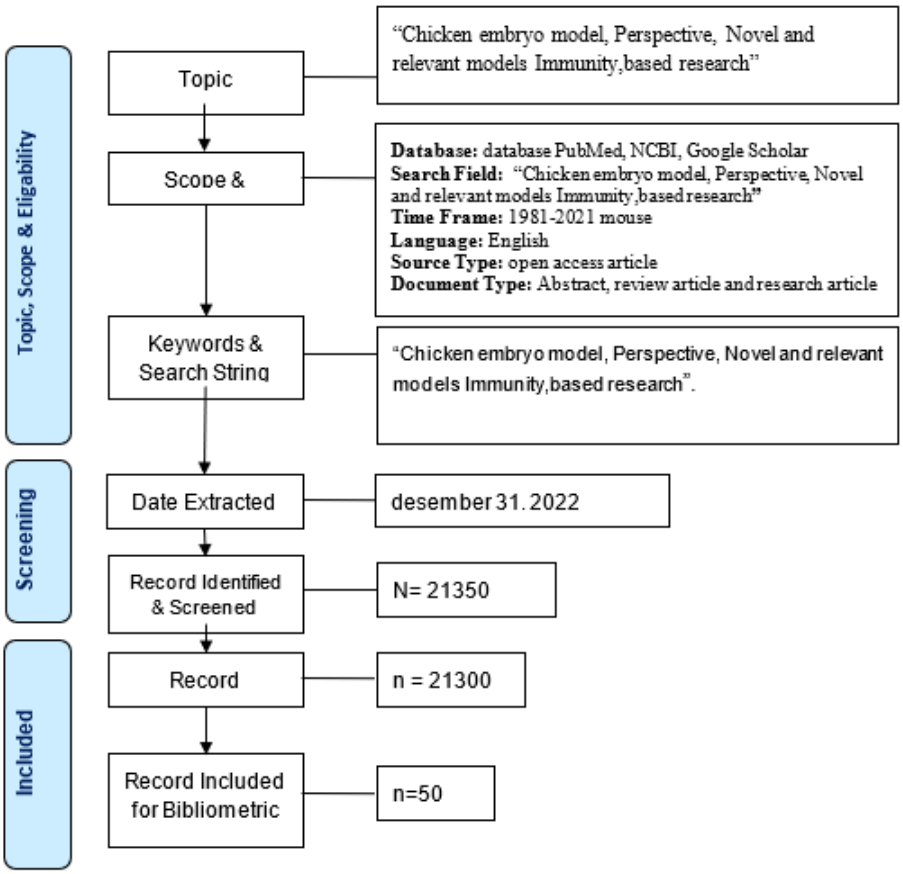

Figure 1. Research strategy flow diagram.

Table 1. Search Strategy Words.

Expression	Meltrin	Embryo
"articulation"OR" formulation"OR"phrasing"OR"statement"OR"utterance"OR"verbalism"OR"voice,"OR"wording"	"A Disintegrin and Metalloproteinase Domain 9 (Meltrin Gamma) Gene"OR" A Disintegrin and Metalloproteinase Domain 9 Gene"OR"ADAM Metallopeptidase Domain 9 (Meltrin Gamma) Gene"OR"ADAM Metallopeptidase Domain 9 wt Allele"OR"ADAM9 wt Allele"OR"Cone Rod Dystrophy 9 Gene"OR"CORD9"OR"KIAA0021"OR"MCMP"OR"MDC9"	"budding"OR"germinal"OR"infant"OR"ancient"OR"early"OR"primal"OR"primeval"OR"primitive"OR"primordial"OR"aged"OR"age-old"OR"antediluvian"OR"antiquated" OR"antique"

4. RESULTS AND DISCUSSION

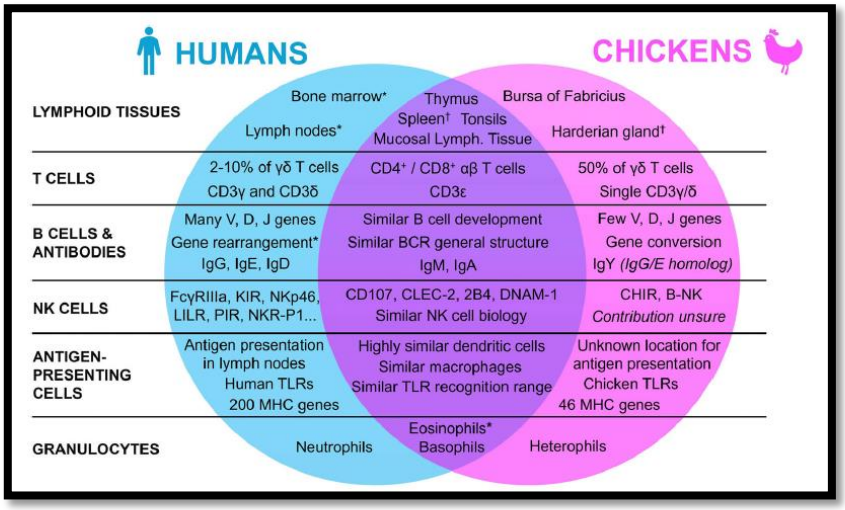

Figure 1. "Summary of the similarities and variations among the human and the hen immune systems.

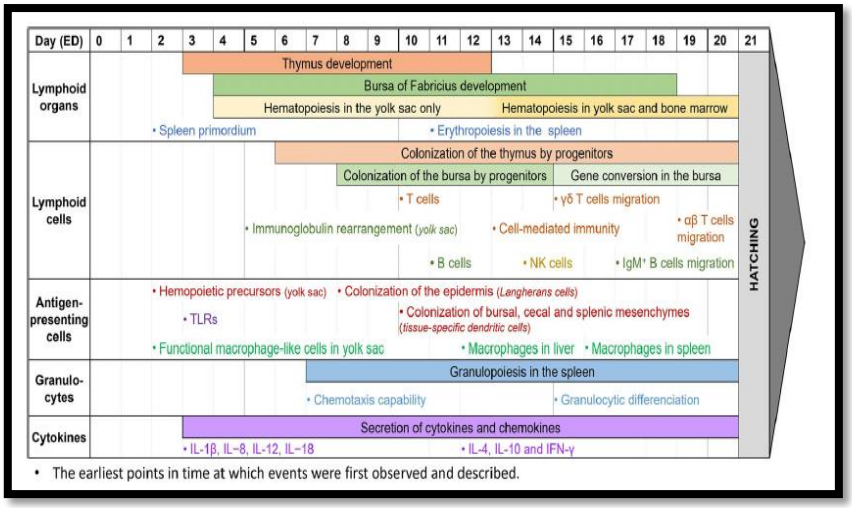

Figure 2. Features of the immune system observed during chick embryogenesis. reserve: This figure summarizes observations reported in the scientific literature. It corresponds to a specific study performed at a specific time point in each case and does not represent the degree of characterization of the immune system during embryogenesis. that's right Most studies do not cover the entire developmental period and therefore cannot be interpreted as an accurate description of the development of the in-ovo immune system.

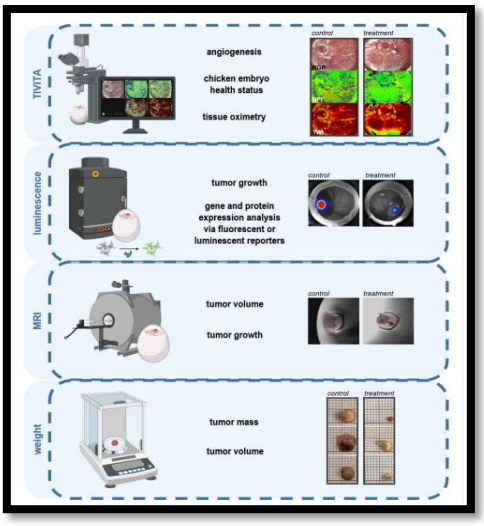

Figure 3. In vivo monitoring of angiogenesis, tumor growth, and assessment of tumor weight using chicken models and immunological parameters.

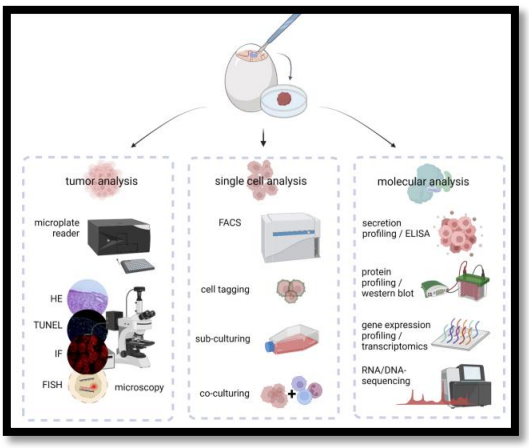

Figure 4. Downstream analysis of resected oocyte-proliferating tumors at the gross, cellular, molecular and immunological levels.

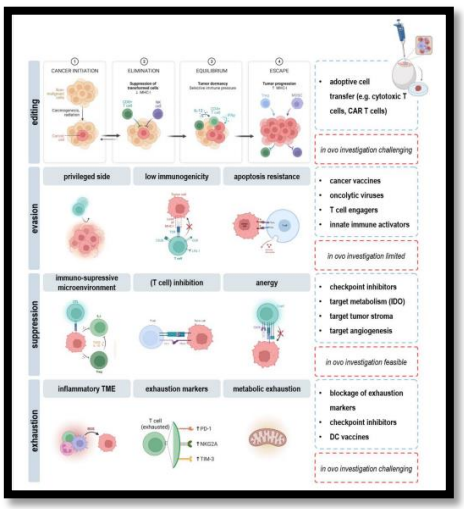

Figure 5. Applicability and limitations of in ovo models in immuno-oncology research.

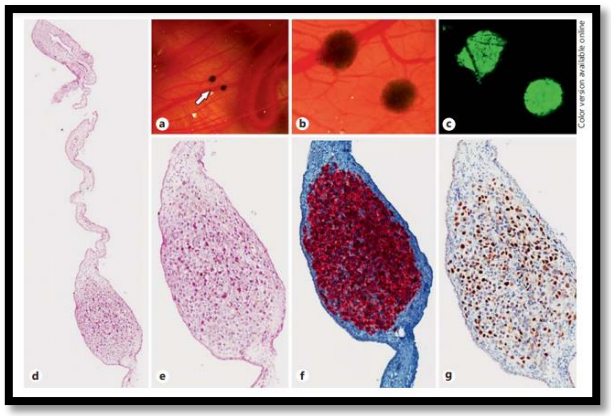

Figure 6. Gross detection and immunohistochemical analysis of tumor nodules formed by the CAM assay.

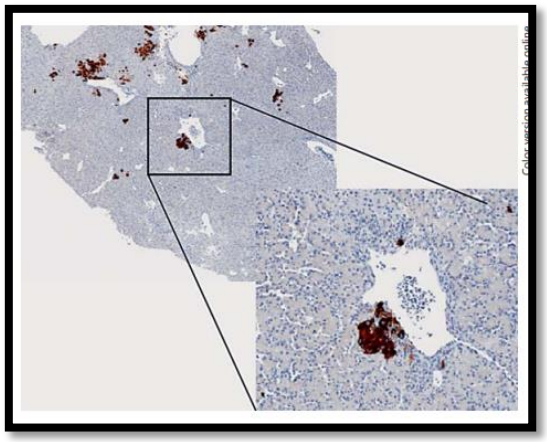

Figure 7. macroscopic detection and immunohistochemical analysis of Choroidal melanoma foci in chickens embryonic liver.

According to **Figure 2., Figure 3., Figure 4., Figure 5., Figure 6., Figure 7.;** and **Figure 8.;** A proper immunological response takes time to develop in chickens, as in other species. The vertebrate immune system utilizes various cell types. All living things are interdependent. Through a number of intermediaries, this system provides excellent disease protection. For the average person, immunity is the primary immune response. Specifically, it distinguishes between two types of immune responses: adaptive and innate. For immediate immunization, various cell types, including B cells, are used. Immune cells such as natural killer (NK) cells, dendritic cells, granulocytes, and macrophages eliminate infections, although infections do not discriminate between infected cells. Adaptive immunity takes time to develop. With antigen exposure, it targets B and T cells within a few days. This process begins with antigen delivery by innate immune cells such as dendritic cells and macrophages. Activation of helper T cells and antigen-specific antibodies allows vertebrates to generate a comprehensive and effective defense when faced with a specific threat (Cabeza-Cabrerizo et al., 2021; Kaspers & Kaiser,

2014; K. Murphy, 2016; Oláh et al., 1996; Rehman et al., 2017; Rhga et al., 2020; Wu & Kaiser, 2011; Yun et al., 2021).

Also as supported on **Supplementary Tabel 1**., a proper understanding of chicken immunity is crucial for accurately describing the most important immune cell types. The distance between these two sites has remained unchanged for over 330 million years. Chickens and their human ancestors face similar ecological niche challenges. Some microbes may possess the ability to trigger immune responses. Although the lymphatic systems of different organs are unique, there must be significant variation among them. The chicken appears simple yet practical. The respiratory system is the same. The chicken model is now operational. This remarkable work has enriched our knowledge of immunology. It has been a standard in immune system research for some time. Models created from chicken embryos have recently seen a surge in demand. Compared to alternatives, these models are superior in efficiency, affordability, and ease of use. Some potential applications include assessing angiogenesis, tumor size, tumor growth, and the effectiveness of metastatic therapies. There are many issues with these models, and they are not sufficient to replace the Classical Preclinical Models. These models have the potential to bridge the gap between basic cells and complex organisms. This strategy, in general, prioritizes the three Rs. These models are particularly useful for immune system studies conducted during the first ten days of embryogenesis, as they highlight the stages that immunologically imperfect embryos may go through to still develop a robust immune response. However, the avian immune system appears to be unique. That people react differently to the immune system is an important part of this concept. These concerns aside, this model appears to be a powerful tool for investigating inflammation and immunology, and may hold the key to confirming many molecular features (Rhga et al., 2020; Sutton et al., 2021; T-P et al., 2014, 2015; Wu & Kaiser, 2011)

5. CONCLUSION AND SUGGESTIONS

Of the 21,300 articles searched for relevant publications in PubMed, NCBI, and Google Scholar, 50 were deemed suitable for inclusion. Nevertheless, this model provides a wealth of information for researchers interested in inflammation and immunology, and may be the most effective approach for examining different parts of the molecule.

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