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ARTICLE

Observations Biomedicals in Veterinary Pathobiology

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Abstract

Observations in biomedicals within veterinary pathobiology encompass the study of disease mechanisms and pathological conditions affecting animals, bridging the gap between veterinary science and biomedical research. This field focuses on understanding the cellular, molecular, and genetic basis of diseases in animals, providing critical insights that enhance diagnostic and therapeutic approaches. Key areas include infectious diseases, cancer, immunopathology, and genetic disorders. Advanced techniques such as molecular diagnostics, histopathology, and imaging are utilized to investigate these conditions. The integration of biomedical research in veterinary pathobiology not only improves animal health and welfare but also contributes to comparative medicine, where findings in animal models can inform human medical research. Observational studies and clinical trials in this field help identify disease patterns, emerging pathogens, and the efficacy of new treatments. This multidisciplinary approach ensures a comprehensive understanding of animal diseases, fostering advancements in both veterinary and human healthcare.

Keywords: Comparative Medicine; Disease Mechanisms; Molecular Diagnostics; Pathological Conditions; Veterinary Science

Abbreviations: BSH: Bile Salt Hydrolase, VBSC: Veterinary and Biomedical Sciences, VTPB: Veterinary Pathobiology

1. Introduction

Delving into the realm of biomedicals, the field of veterinary pathobiology encompasses a wide array of disciplines, including microbiology, pathology, immunology, and infectious diseases. At Texas A&M University, the Veterinary Pathobiology (VTPB) courses offer a comprehensive curriculum that equips students with a profound understanding of animal health, disease processes, and the intricate relationship between biomedicals and veterinary sciences [1, 2, 3]. These courses, spanning undergraduate, graduate, and professional levels, cover fundamental concepts in pathobiology, fermentation and gastrointestinal microbiology, immunogenetics, comparative immunology, molecular methods for microbial detection, and biomedical engineering. Additionally, they explore specialized areas such as phlebotomy, urology, thrombosis, and the intricate interplay between people, animals, plants, and the environment through a One Health approach [4, 5, 6] (Fig. 1).

1.1 Fundamental Concepts

Veterinary biomedical sciences is an interdisciplinary field that combines veterinary and biomedical sciences, focused on animal and human well-being, disease prevention and treatment. Key research areas in this field include:

1. Gene therapy

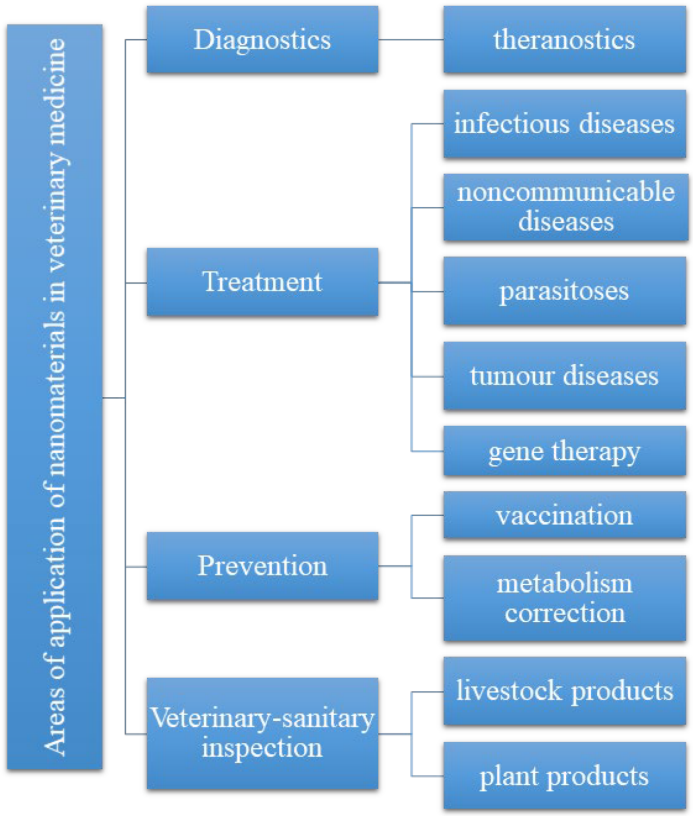

Figure 1. Main application areas of nanomaterials in veterinary medicine.

2. Biomedical diagnosis
3. Biomedical sensors
4. Biomedical signal and image processing
5. Biomarker discovery
6. Biomedical engineering
7. Implantable biomedical devices
8. Biomaterial research
9. Molecular veterinary
10. Pathogenesis and mechanisms of diseases

The Veterinary Science program at the University of Nebraska-Lincoln provides a broad knowledge of anatomy, biochemistry, histology, immunology, molecular biology, pathology, pharmacology, toxicology, and virology as they relate to diverse mammalian species (Fig. 2). Notable courses in this program include:

- Success in Veterinary Science
- Animal Physiological Systems
- Breeds, Signalment and Vitals of Domestic Animals
- Principles and Prevention of Livestock Diseases
- Wildlife Health

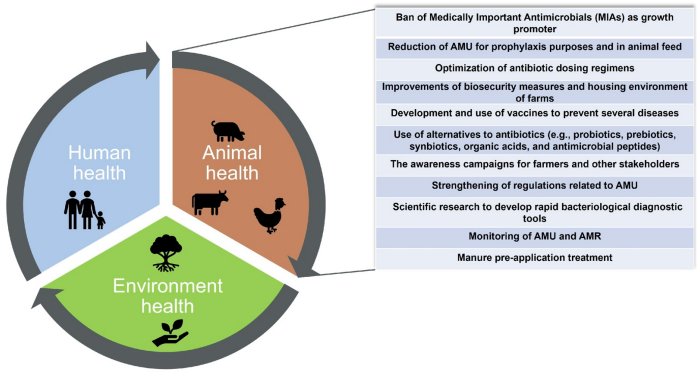

Figure 2. Actions conducted in livestock to tackle antimicrobial resistance from a One Health perspective.

- Pathogenic Microbiology

The Veterinary and Biomedical Sciences (VBSC) program covers a wide range of topics related to fundamental concepts in veterinary science and biomedical sciences. These include mechanisms of disease, the immune system, toxicology, cancer research, pharmacology, public health, and more. The VBSC program offers undergraduate courses at various levels, covering a comprehensive curriculum in veterinary and biomedical sciences [7, 8, 9, 10].

2. Veterinary Pathology

Veterinary pathology encompasses a wide range of research and clinical applications aimed at understanding and treating diseases in animals. Recent advancements in this field have led to innovative therapies, diagnostic techniques, and insights into disease mechanisms (Fig. 3).

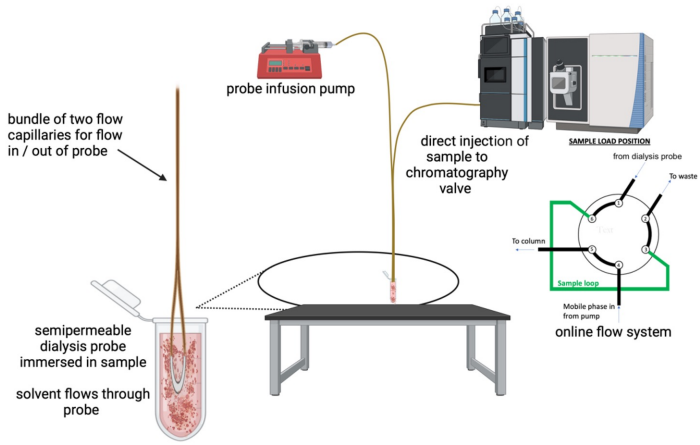

Figure 3. The experimental apparatus for green and automated sample cleanup prior to LC-MS.

1. **Novel Treatments and Therapies**:
   - Low-dose radiation therapy has shown promising results in treating Feline Idiopathic Cystitis, with all cats in a study exhibiting improvement and most never experiencing another episode.
   - The development of an inhalable powder called SHIELD can reinforce the body's mucosal layer,

reducing viral invasion and infection in animal models.

- Research is underway to develop a probiotic-based oral vaccine for clostridial dermatitis in turkeys, a disease that has proven challenging to control.

2. **Diagnostic and Monitoring Techniques**:
   - Measuring gait speed in senior dogs can serve as an indicator of cognitive decline and dementia, as slower walking speed is associated with declining neurological function.
   - Analyzing DNA from medieval parchment manuscripts can provide insights into animal husbandry, agricultural history, and other aspects of medieval life.
   - A genetic database of North Carolina's black bears has been created to assist law enforcement and wildlife officials in identifying bears involved in poaching or human-bear interactions.
3. **Microbiome and Disease Pathogenesis**:
   - Certain enzymes called bile salt hydrolases (BSHs) can restrict Clostridioides difficile (C. diff.) colonization by altering bile acids in the gut microbiome, leading to potential 'designer' probiotics to protect against disease.
   - Research has found that a cat's gallbladder does not have its own microbiome, an important discovery for treating inflammatory diseases.
   - Studying the role of unclean vehicles in transmitting swine coronavirus could lead to better sanitization methods to prevent outbreaks.

Furthermore, a special issue of the journal 'Animals' focuses on recent advances in veterinary pathology, inviting submissions on various aspects of the pathology of diseases in domestic animals, laboratory animals, and wildlife species. Institutions like the College of Veterinary Medicine at NC State University and the Department of Veterinary Pathology at Iowa State University offer comprehensive programs and research opportunities in veterinary pathobiology, training students and professionals in areas such as disease mechanisms, pathology, clinical pathology, toxicology, and parasitology [11, 12, 13, 14, 15].

3. Diagnostic Techniques

Histological examination of biopsies plays a crucial role in disease diagnosis in veterinary pathobiology. Pathologists can often make a definitive diagnosis by examining biopsies under the microscope. They analyze a wide variety of samples, including those from dogs, cats, small mammals, horses, farm animals, birds, and zoo animals. Common sample types include skin, oral cavity, and mammary glands. While many cases allow for a definitive diagnosis, some samples cannot be assigned a final diagnosis. In such cases, pathologists discuss potential differential diagnoses and suggest additional tests that may be helpful [16] (Fig. 4).

Diagnostic techniques in veterinary pathobiology encompass various laboratory tests and analyses, each providing valuable insights into animal health and disease processes. These include:

1. **Clinical Chemistry**: Analyzes the chemical composition of blood and other body fluids to determine organ function and identify specific disorders.
2. **Cytology**: Involves the study of individual cells to identify cell types, including cancerous cells, and detect the presence of infectious agents.
3. **Fluid Analysis**: Examines bodily fluids other than blood, like urine or joint fluid, to check for cells and proteins.
4. **Hematology**: Studies the blood cellular elements, providing information about anemia, inflammation, and clotting.
5. **Histology**: Involves the microscopic study of animal tissue structure to determine if it is normal

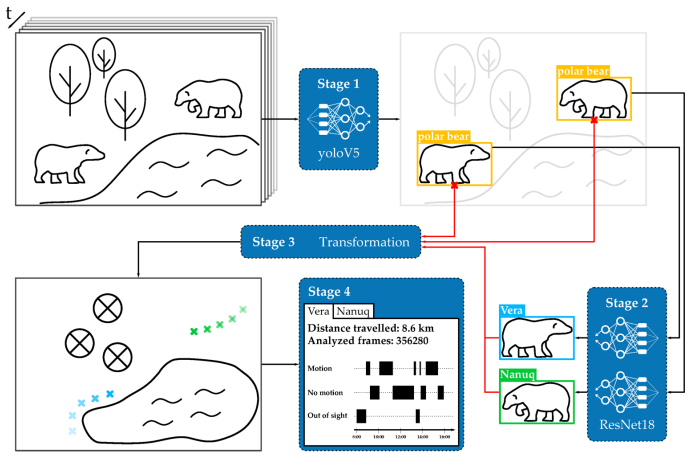

Figure 4. A high-level overview of the proposed framework.

or diseased.

6. **Microbiology**: Studies bacteria, viruses, fungi, and other microorganisms, and tests can culture and identify microbes and test their sensitivity to antibiotics.
7. **Serology**: Measures levels of antibodies in blood serum and other body fluids to detect exposure to infectious agents.
8. **Toxicology**: Studies poisons and their effects on animals, and tests identify the poison and extent of damage if a pet is suspected of poisoning [17].

Advancements in veterinary pathology are moving towards a more objective approach, incorporating new tools like molecular techniques, digital image analysis, and quantitative pathology. Molecular diagnostics have led to a better understanding of the pathobiology, epidemiology, and evolution of viral pathogens affecting animals, some of which have zoonotic potential. The application of next-generation sequencing has allowed for the discovery and characterization of many new viral species in diverse animal hosts. Additionally, new imaging techniques like imaging flow cytometry and histology-directed mass spectrometry are providing novel insights into disease pathogenesis. However, there is a need for more guidelines and consensus statements to standardize veterinary diagnostic testing and reporting [18, 19, 20].

4. Infectious Diseases

Infectious diseases have long been a focal point of pathologic convergence between species, as exemplified by Edward Jenner's pioneering work on using cowpox and horsepox to prevent smallpox in humans. Pathologists play a pivotal role in the One Health approach, serving as a critical component of the multidisciplinary team that diagnoses zoonotic diseases and discovers emerging pathogens [21, 22]. Both human and veterinary pathologists are uniquely positioned to:

1. Identify clusters or trends in patient populations caused by infectious agents, presaging potential outbreaks.
2. Leverage the invaluable repository of tissue samples to investigate a variety of pathogens.
3. Develop and validate diagnostic tests for epidemiologic and clinical use.
4. Provide surveillance data on emerging infectious diseases.
5. Define the pathogenesis and pathology of these new diseases. Moreover, pathologists are instrumental in diagnosing zoonoses that impact the food supply and the economy [23].

The University of Wisconsin School of Veterinary Medicine (SVM) exemplifies the One Health approach in action:

- Awarded $3.7 million from the USDA to develop vaccines preventing coronavirus transmission between animals and humans.
- Conducted studies demonstrating that mRNA vaccines can harness T-cells to combat COVID-19 in the lungs, even against emerging SARS-CoV-2 variants.
- Offered the first-of-its-kind TEACH (Training in Emergency Animal Care and Handling) program for veterinarians in Hyderabad, India.
- Boasts a record-setting research portfolio spanning influenza, human respiratory disorders, multiple sclerosis, and cancer treatments.

As human activity encroaches on wildlife habitats, interspecies transmission of infectious diseases is a growing concern. Veterinary pathologists play a vital role in identifying and investigating these emerging diseases, underscoring the importance of a One Health approach in veterinary pathobiology.

5. Non-infectious Diseases

Advances in genomic mapping and sequencing technologies have revolutionized our understanding of non-infectious diseases in animals. By analyzing the genetic makeup of various species, researchers can identify genetic abnormalities and associations with complex diseases [24, 25, 26]. This has paved the way for early detection, targeted therapies, and improved management strategies for conditions such as:

1. **Inherited Disorders**: Genomic mapping has facilitated the identification of genetic mutations responsible for inherited diseases in animals, including:
   - Degenerative myelopathy in dogs, a progressive neurological disorder caused by a mutation in the SOD1 gene.
   - Polycystic kidney disease in Persian cats, linked to mutations in the PKD1 and PKD2 genes.
   - Glycogen storage disease in horses, caused by mutations in the GYS1 gene.
2. **Cancer**: Advances in cancer genomics have provided insights into the molecular mechanisms underlying various types of cancers in animals. For example:
   - Comparative genomic studies have identified shared genetic alterations in canine and human breast cancers, opening avenues for translational research [27].
   - Genomic profiling has revealed distinct molecular subtypes of lymphoma in dogs, paving the way for personalized treatment strategies [28, 29].
3. **Metabolic Disorders**: Genomic studies have shed light on the genetic basis of metabolic disorders in animals, such as:
   - Diabetes mellitus in dogs, associated with mutations in the insulin gene and other genetic factors [30].
   - Obesity in horses, linked to variations in genes involved in appetite regulation and energy metabolism [31].

Despite these advancements, challenges remain in exploring epigenetic patterns and cancer genomes in animals. Epigenetic modifications, which regulate gene expression without altering the DNA sequence, play a crucial role in disease development and progression. Understanding these mechanisms can provide valuable insights into disease pathogenesis and potential therapeutic targets.

Furthermore, biomedical engineering principles are being applied to veterinary medicine, with the potential for personalized medicine in pets. For instance, the development of implantable devices and biosensors can facilitate real-time monitoring of physiological parameters, enabling early detection and management of various conditions. Additionally, the application of biomedical imaging techniques, such as magnetic resonance imaging (MRI) and computed tomography (CT), has enhanced diagnostic capabilities in veterinary medicine.

Biomedicals play a pivotal role in advancing our understanding and treatment of non-infectious diseases in animals. By integrating genomic data, epigenetic insights, and biomedical engineering innovations, the field of veterinary pathobiology continues to push the boundaries of animal healthcare, ultimately benefiting both animal and human populations through the One Health approach.

6. Comparative Pathology

Animal models of human diseases have been central to the study of pathogenesis and potential treatments, based on the premise of evolutionarily conserved mechanisms. However, reconciling pathology nomenclature between laboratory animals and humans is crucial for integrating genetic association data and understanding common underlying pathobiological processes.

Unfortunately, there is currently a shortage of veterinarians with expertise in laboratory animal medicine and comparative pathology. Veterinarian principal investigators comprise an unsatisfactorily small percentage of all RO1-funded principal investigators. The main reason for this shortage is a lack of commitment from veterinary schools to educate veterinary students and graduates for careers other than private clinical practice. Recommendations to address this issue include:

1. Raising awareness about the importance of comparative pathology
2. Providing more exposure and training opportunities
3. Improving recruitment and curricula
4. Enhancing mentorship programs
5. Addressing financial barriers

The concept of "One Medicine" refers to the idea that all biology has utility for study and knowledge to better understand the human condition. Animal models have been increasingly used for biomedical research, and emerging technologies like gene editing (e.g., CRISPR) and new animal models can improve their efficacy and relevance. However, these advancements also introduce new challenges that need to be addressed [17] (Fig. 5).

The COVID-19 pandemic has illustrated the need for new animal models and approaches for emerging diseases, as well as the critical role of comparative pathologists in developing and interpreting these models. While animal models have been fundamental in preclinical and biomedical research, concerns have been raised about their limitations and ability to reliably predict clinical trial success.

Veterinary pathologists play a crucial role in biomedical research teams, providing expertise in study design, tissue collection and processing, and data interpretation. Effective communication and education of research teams by pathologists is essential to achieve useful, reproducible, and replicable results. Pathologists need to recognize the limitations of animal models and manage expectations, as well as address challenges like "Do-It-Yourself" pathology by researchers. Opportunities exist for pathologists to advance their roles and contributions in biomedical research, particularly in emerging areas like gene editing and pandemic response.

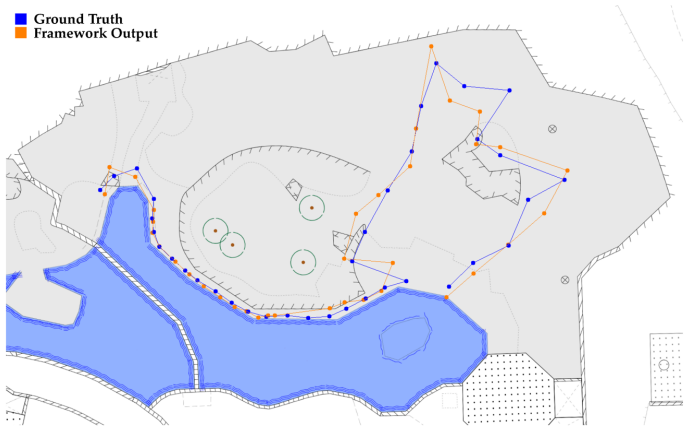

Figure 5. Graphical representation of the result of experiment 6

7. One Health Approach

The 'One Health' concept aims to integrate principles and discoveries in both veterinary and human medicine for the mutual benefit of all species. This approach recognizes the interconnectedness of human, animal, and environmental health, and the need for collaborative efforts to address complex health challenges.

The roots of the 'One Health' concept can be traced back to the 'One Medicine, One Pathology' concept, developed over a century ago by Rudolf Virchow and William Osler. This concept emphasizes the lack of a dividing line between animal and human medicine, as many diseases and pathological processes are shared across species. Veterinary pathologists like Thomas Carlyle Jones and George Migaki have been major advocates of this concept, and their work has served as a prototype for many books on animal models of human diseases [21].

Collaborative efforts involving animal models have led to significant breakthroughs in human medicine. For instance, the development of a recombinant vaccine to prevent oral papillomavirus infection in dogs has paved the way for similar vaccines in humans. Such successes highlight the importance of fostering a new generation of experimental pathologists and physicians trained to think across species, a key challenge for veterinary and human medical schools (Fig. 6).

The 'One Health' approach encompasses several key principles:

1. **Interdisciplinary Collaboration**: Effective communication and collaboration among veterinarians, physicians, researchers, and other stakeholders are essential for addressing complex health issues that span multiple domains.
2. **Comparative Medicine**: Studying diseases and pathological processes across different species can provide valuable insights and inform the development of diagnostic tools, treatments, and preventive measures.
3. **Environmental Considerations**: Environmental factors, such as climate change, habitat destruction, and pollution, can have significant impacts on the health of humans, animals, and ecosystems. Addressing these factors is crucial for promoting overall health and well-being.
4. **Zoonotic Disease Prevention**: Many emerging infectious diseases, such as COVID-19, have zoonotic origins, highlighting the importance of surveillance, early detection, and prevention strategies that involve both human and animal populations.
5. **Antimicrobial Resistance**: The overuse and misuse of antibiotics in both human and veterinary

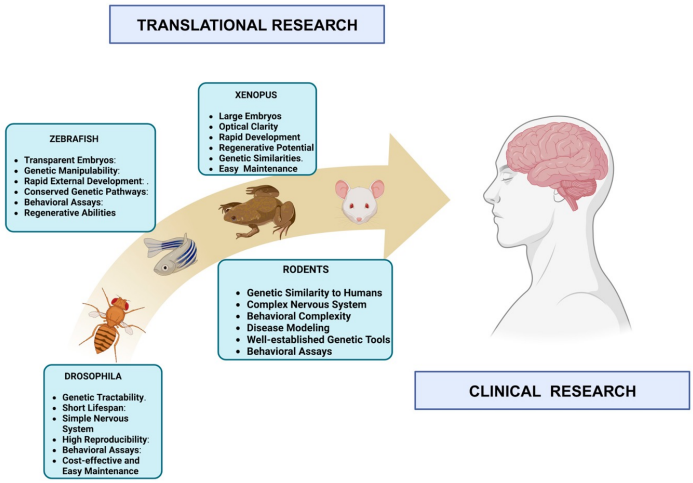

Figure 6. From lab to clinic

medicine contribute to the global threat of antimicrobial resistance. A 'One Health' approach is necessary to develop strategies for responsible antibiotic use and the development of alternative therapies.

By embracing the 'One Health' concept, the field of veterinary pathobiology can play a vital role in advancing our understanding of disease mechanisms, developing innovative treatments, and promoting the overall well-being of humans, animals, and the environment.

8. Research and Advancements

Biomedical research and advancements in veterinary pathobiology are rapidly progressing, driven by interdisciplinary collaborations and cutting-edge technologies. Here are some notable areas of research and advancements in this field (Fig. 7):

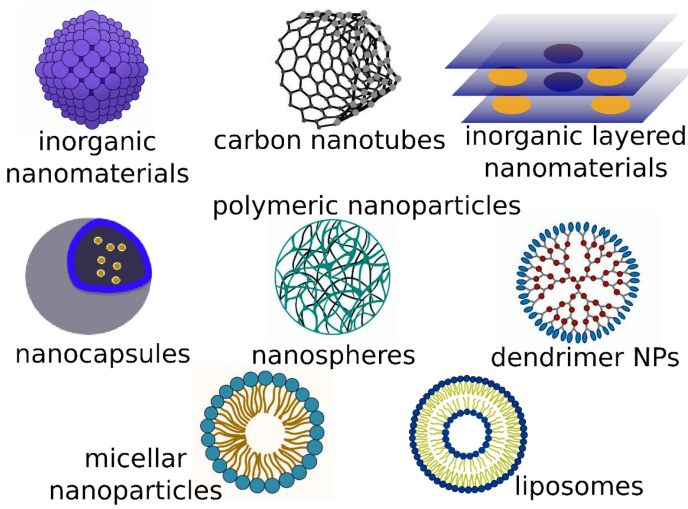

Figure 7. Types of nanoparticles used in veterinary medicine and livestock husbandry.

1. **Genomics and Precision Medicine**:
   - Whole-genome sequencing and analysis are enabling the identification of genetic markers associated with disease susceptibility, progression, and treatment response in various animal species.
   - This paves the way for personalized medicine approaches, where treatments can be tailored based on an individual animal's genetic profile.
   - For example, researchers at the University of Pennsylvania have developed a genetic test to identify dogs at risk for developing a severe form of inflammatory bowel disease (IBD), allowing for early intervention and management strategies [32].
2. **Biomarkers and Diagnostic Tools**:
   - Researchers are actively exploring novel biomarkers for early disease detection, monitoring, and prognosis in animals.
   - Advances in proteomics, metabolomics, and other "omics" technologies are facilitating the discovery of these biomarkers.
   - For instance, a study at the University of Georgia identified a panel of protein biomarkers in dogs that could potentially differentiate between various types of cancers, aiding in early diagnosis and treatment planning [33, 34].
3. **Regenerative Medicine and Tissue Engineering**:
   - Stem cell therapy and tissue engineering hold great promise for treating various conditions in animals, including orthopedic injuries, neurological disorders, and organ failure.
   - Researchers at the University of California, Davis, have developed a regenerative therapy using stem cells derived from fat tissue to treat osteoarthritis in horses, with promising results in clinical trials [35].
   - Additionally, bioengineered scaffolds and biomaterials are being explored for tissue repair and regeneration in various animal models.
4. **Vaccine Development and Immunotherapies**:
   - Advances in immunology and vaccinology are driving the development of novel vaccines and immunotherapies for both infectious and non-infectious diseases in animals.
   - For example, researchers at the University of Wisconsin-Madison have developed a DNA vaccine against canine oral melanoma, a highly aggressive form of cancer in dogs, with promising results in clinical trials [36, 37].
   - Immunotherapies, such as monoclonal antibodies and checkpoint inhibitors, are also being explored for the treatment of various cancers in companion animals.
5. **Antimicrobial Resistance and Alternative Therapies**:
   - The rise of antimicrobial resistance in both human and veterinary medicine has prompted researchers to explore alternative therapies and strategies to combat infectious diseases in animals.
   - This includes the development of novel antimicrobial agents, phage therapy, and the use of probiotics and other microbiome-based approaches.
   - For instance, researchers at the University of Guelph have investigated the use of bacteriophages (viruses that infect bacteria) as a potential alternative to antibiotics for treating bovine mastitis, a common and costly disease in dairy cattle [38].

These are just a few examples of the ongoing research and advancements in the field of veterinary pathobiology, driven by the integration of biomedical sciences and the One Health approach. Interdisciplinary collaborations and the application of cutting-edge technologies are paving the way for

improved disease prevention, diagnosis, and treatment strategies, ultimately benefiting both animal and human health.

9. Conclusion

The field of veterinary pathobiology lies at the intersection of biomedical sciences and animal health, offering a comprehensive understanding of disease processes, diagnostic techniques, and innovative therapies. By embracing the One Health approach, this multidisciplinary field recognizes the interconnectedness of human, animal, and environmental health, fostering collaborative efforts to address complex challenges. Through advancements in genomics, regenerative medicine, vaccine development, and antimicrobial research, the field of veterinary pathobiology continues to push boundaries, ultimately benefiting both animal and human populations. The integration of cutting-edge technologies and interdisciplinary collaborations paves the way for improved disease prevention, diagnosis, and treatment strategies, underscoring the vital role of this field in promoting overall well-being.

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