Summary

The One Medicine project took advantage of existing expertise and infrastructure at MSU and UM to expand efforts in addressing contemporary animal and human health challenges most critical to Montana. The funding requested was $1,500,000 and was distributed over one primary area of economic and public health importance, addressing major emphasis areas of the Montana Research Initiative: Health and Biomedical Sciences and Agriculture (livestock). The research goal/focus was to develop new therapeutics that can ***reduce the impacts of inflammatory and infectious diseases on animal and human health.*** The proposal capitalized on highly focused and well-established research programs that have strong records of success in biomedical research to enhance research capacity and empower these programs to translate basic biological research into new therapeutic approaches that address important Montana health challenges. Key outcomes are listed below with final metrics included in the pages following.

Key Outcomes:

- The research was conducted by 21 investigators and the return on investment was ~ 2.7 to 1 with over $4,000,000 in external funding received. Over $8,000,000 in funding is pending.

- Montana's investment did support translational medicine and helped move four projects from basic science into the small business market through collaboration with the private sector. This included partnerships with two Montana-based companies and fostered the development of a new Montana company. Importantly, all four of these projects are continuing to work with the private sector.

- The funding provided employment through the addition of research staff and the creation of new jobs in the private sector. Overall the project employed a total of 70 full- and part-time individuals.

- The funding resulted in findings that were reported in peer-reviewed publications. Results were also disseminated to the public at multiple local, national and international meetings.

One Medicine

Total Additional Grants Received:

- PI: Agnieszka Rynda-Apple, Co-PI: Mark Jutila, NIH R21. Title: Development of a novel, safe and efficacious *Coxiella burnetii* vaccine, $396,000.
- PI: Mark Jutila, NIH R21. Title: Role of type I IFN and human TLR4 in *Coxiella burnetii* pathogenesis, $396,000.
- PI: Jodi Hedges, NIAID/NIH Center of Biomedical Research Excellence in Zoonotic and Emerging Infectious Diseases. Title: Effect of type I IFN on TLR4 responses in *Coxiella burnetii* infection, $50,000
- PI: Agnieszka Rynda-Apple, NIAID/NIH Center of Biomedical Research Excellence in Zoonotic and Emerging Infectious Diseases. Title: Utilizing VLPs to understand predisposition to secondary bacterial pneumonia, $30,000.
- PI: Raina Plowright, US Geological Survey. Title: USGS Wildlife disease risk analyses, $59,991.
- PI: Ben Lei, NIAID/NIH Center of Biomedical Research Excellence in Zoonotic and Emerging Infectious Diseases. Title: Innate Immune Protection of the Vascular System against *Streptococcus pyogenes*, $30,000.
- PI: Raina Plowright, NIAID/NIH Center of Biomedical Research Excellence in Zoonotic and Emerging Infectious Diseases. Title: Elucidating pulses of bat-borne zoonotic viruses, $50,000.
- PI: Matthew Taylor, NIAID/NIH Center of Biomedical Research Excellence in Zoonotic and Emerging Infectious Diseases. Title: Analysis of West Nile virus neuroinvasive spread, $50,000.
- PI: Diane Bimczok, NIAID/NIH Center of Biomedical Research Excellence in Zoonotic and Emerging Infectious Diseases. Title: Epithelial pathogenesis of *Helicobacter suis* infection, $50,000.
- PI: Mike Minnick, NIH R21. Title: *Caenorhabditis elegans* infection model for *Coxiella burnetii*, $398,750.
- PI: Doug Kominsky, NIH R01. Title: Inflammation-dependent methylation in the mucosa, $250,000.
- PI: Mark Quinn, Pfizer ASPIRE Investigator Initiated Research Grant. Title: Development of Novel JNK Inhibitors for Treatment of Rheumatoid Arthritis, $150,000.
- PI: Raina Plowright, Defense Advanced Research Projects Agency Young Faculty Award. Title: Modeling Pathways to Zoonotic Spillover, $499,999.
- PI: Matthew Taylor, NIAID/NIH Center of Biomedical Research Excellence in Zoonotic and Emerging Infectious Diseases. Title: Inflammatory responses during alphaherpes infection, $40,000.
- PI: Jovanka Voyich, NIAID/NIH Center of Biomedical Research Excellence in Zoonotic and Emerging Infectious Diseases. Title: The SaeR/S Regulatory System of *Staphylococcus aureus* Prevents Complement-mediated Interactions with Human B cells, $40,000.
- PI: Seth Walk, NIAID/NIH Center of Biomedical Research Excellence in Zoonotic and Emerging Infectious Diseases. Title: Novel, narrow-spectrum inhibitors of *Clostridium difficile*, $45,000.
- PI: Blake Weidenheft, NIAID/NIH Center of Biomedical Research Excellence in Zoonotic and Emerging Infectious Diseases. Title: CRISPR generated human genome knockout libraries for studying infectious diseases, $45,000.

- PI: Mary Miles, USDA NIFA. Title: Determining the Gut Microbiota-dependent Impacts of Anthocyanin-rich Aronia Berries on Obese Individuals of Distinct Inflammatory Phenotypes, $150,000.
- PI: Mike Minnick, NIH R21. Title: Small regulatory RNAs of *Bartonella bacilliformis*, the agent of Carrión's disease, $406,517.
- PI: Jovanka Voyich, NIH R21. Title: The SaeR/S Regulatory System of *Staphylococcus aureus* Prevents Complement-mediated Interactions with Human B cells, $396,000.
- PI: Robin Gerlach, Burroughs Wellcome Fund Collaborative Research Travel Grant Program. Title: Linking engineering and urology towards a better understanding and improved treatment of urinary stones. (Role: Mentor), $10,667.
- PI: Valerie Copié, NSF-MCB. Title: Microbial Dark Matter: Forging new discoveries in metabolism, $535,000.

Total Funding Received:

$ 4,078,924

Additional Grants Submitted

- Co-PI: Voyich; NIH R01 Regulation of *Streptococcus pyogenes* virulence by ADP-ribosyltransferase SpyA $180,000.
- Sponsor: Weidenheft; NIH NRSA postdoctoral fellowships (2), Cancer Research Institute – postdoctoral fellowship, NSF- postdoctoral fellowship
- PI: Quinn; NIH R21, Novel JNK Inhibitors for Treatment of Rheumatoid Arthritis, $396,000
- PI: June; NIH R21, NEOPS: Nanostructure-Enhanced Optical Pressure Sensors for Mouse Knees, $395,903
- PI: June PI; NIH R21, Advanced NMR Evaluation of Fluid Motion in Human Articular Cartilage for Improved Diagnosis of Osteoarthritis, $395,927
- PI: Voyich; NIH R01. Sensing and Adapting to the Neutrophil: Determining SaeR/S Dependent Evasion Strategies Used by *Staphylococcus aureus*, $1,821,360.
- PI: Voyich; NIH R21 Influence of Antecedent Influenza A Infection on *Staphylococcus aureus* Virulence Gene Expression during Pneumonia, $396,000
- PI: Lei; NIH R01 Innate Immune Evasion by Group A *Streptococcus*, $1,821,360
- PI: Bimczok; NIH R01 Mechanisms of Dendritic Cell-Epithelial Cell Interactions in Human Gastric Mucosa, $1,821,360
- PI: Copié; NIH R21 Modulation of *S.aureus*-neutrophil interactions and evasion of neutrophil killing through metabolic reprogramming, $396,000.
- PI: Bimczok; NIH R21 "Phenotypic and transcriptional classification of dendritic cell and macrophage subsets in human gastric mucosa", $396,000.
- PI: Jutila; NIH R21 Protective role for type I interferon in *Clostridium difficile* infection $396,000.

Partnerships with Industry:
Worked with 2 Montana Companies and Generated 1 New Company

- The three main PIs of the One Medicine proposal (Voyich, Jutila, and Quinn) worked with Totem Biosciences to generate data and projects appropriate for SBIR and STTR grants.
- PI Quinn established a collaboration with a small Montana pharmaceutical company, SAJE Pharma, LLC from Kalispell, MT. SAJE has been developing novel inhibitors of

S-nitrosoglutathione reductase (GSNOR) as anti-inflammatory treatments. Tested a combination of JNK and GSNOR inhibitors in a model of rheumatoid arthritis and found that both compounds were individually effective, but that the combined treatment with both compounds was even better at inhibiting the development of rheumatoid arthritis. Further studies are being planned and an STTR proposal submission is planned for September 2017.

- An SBIR was submitted with Totem for investigating scours. This grant is still pending.
- Two additional SBIR applications are in progress with Totem investigating inflammatory mediators and immunomodulation to combat *Staphylococcus aureus.*
- MREDI support allowed the Weidenheft lab to establish a genome wide screening method that has become the foundation for an R&D biotechnology company called SurGene, LLC that founded by Dr. Weidenheft in 2016 and received funding from Amgen in 2017. SurGene is currently in the final stages of negotiating a contract that will employ 2 to 3 scientist, with the goal of developing new molecular tools that enhance the Surgical repair of defective Genes.

Disseminating Knowledge Gained from the State Funded Initiative:

- Total papers with citation 16
- 13 Public Talks/Seminars Highlighting One Medicine
- One Medicine was highlighted at the Montana Agricultural Symposium (Montana State University) breakout groups with Montana Stockgrowers resulted invite of One Medicine researchers to present *The Domestic and Wild Sheep Symposium February 9 and 10, 2017.* This symposium was sponsored by the Montana Wool Growers Association, Montana Wild Sheep Foundation, and Montana Fish, Wildlife and Parks.

Patents or Commercial Products Developed:

- None. However, SBIR and STTR applications may lead to commercialization of products

Jobs Created:

- Private sector: 2
- Research Scientists/Faculty: 7 less than full time; 3 full time
- Technicians: 11 less than full time; 7 full time
- Postdoctoral fellows: 5 less than full time; 3 full time
- Grad Students: 14
- Undergraduate Students: 18