

## TCR Proposal Submission - KarlMcmanus

### Case

If the response to both questions below is 'No', a TCR Proposal should not be developed. If you have selected 'no' for both questions, the remainder of the form will be restricted.

Is there a link to NHMRC or Australian Government priorities, including Aboriginal and Torres Strait Islander Health, and/or to Ministerially-agreed State and Territory health research priorities?:

Yes

If there is no link to the above mentioned priorities, does the TCR address a disease area with a significant research knowledge gap or unmet need?:

Yes

### Proposed Research Question

Provide a clear statement of the research question that would be addressed if the proposal was to be progressed.

**For example: This TCR aims to support research that addresses the following research question: How can young adults be engaged and retained in successful interventions that lead to healthy eating and a reduced risk of obesity for Australians?**

Tick borne infections have been neglected in Australia for over 20 years. The significance of their contribution to chronic diseases have been ignored. It is time for more attention, research into tick borne diseases is undertaken in Australia. There is an urgent need to identify tick borne pathogens that are infectious in people and develop diagnostics and better treatment protocols. This will enable less people becoming chronically ill as tick borne infections have non-specific symptoms and are multi systemic, hence difficult to diagnose clinically and unreliable diagnostics.

### Submitting Organisation

Provide details of the organisation(s) that endorse this proposal, noting that proposals from individuals, without the support of a community or professional group, will not be considered by the committee.

Karl McManus Foundation (KMF) was founded in memory of Karl who passed away from complications of tick borne diseases in 2010. The aim of KMF is to raise awareness of tick borne diseases, erode barriers to diagnosis and treatment by encouraging education and funding research in Australia. KMF is a crucial organisation with extensive knowledge and experience in tick borne diseases in Australia. KMF funds research in the Tick Borne Diseases Unit, School of Medical Sciences (Pharmacology), University of Sydney and has hosted tick borne diseases conferences with international plenary speakers in 2013-2015.

Directors of KMF are:

Prof. David Irving

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Emeritus Prof Tim Roberts

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This document is submitted by Dr Mualla McManus. The founding director of KMF

## Section 1

The proposed TCR must address a significant research knowledge gap or unmet need within the disease area. There must be the potential to greatly advance our understanding of the issue in the disease area.

Make a case for how the proposed TCR addresses a significant research knowledge gap, giving consideration to the following guidance questions:

### What is the current disease status?

Prevalence;

Burden of disease on the individual and community (mortality and morbidity, DALY/QALY, financial cost, lifestyle);

Burden of disease on the health system and Australian economy.

### What is the current research effort in the disease area?

How much research is being done in the disease area?

Current NHMRC, and other, funding?

What is the current research capacity and capability in the discipline?

Are there new and/or novel treatments available?

When was the last breakthrough?

Current status of tick borne diseases (TBD) in Australia is an emerging infections lacking research and understanding. It is embroiled in controversy as Lyme disease terminology dominates media coverage while the true nature of this serious chronic infectious disease/syndrome is lost in translation.

Currently the focus is on the existence of disease causing *Borrelia* in Australian ticks. The overseas acquired TBD excluding Lyme disease is poorly diagnosed too. Most patients with TBD have travel history but have not being diagnosed early to be treated appropriately.

There are clearly pathogens in Australian ticks causing illness in people. Their nature type and virulence is unclear. There is urgent need for research to establish TBD as mainstream disease in Australia and to remove the controversy, and the Lyme disease lexicon so people can be diagnosed and treated appropriately early, regardless of where they have acquired it. Chronic TBD need to be prevented for future generations.

Prevalence: TBD in Australia are currently undefined and diagnosis is not possible purely from clinical symptoms since these are non-specific and multi-systemic, and the diagnostics used in Australia are dominated by the USA Lyme disease *Borrelia* proteins. Therefore an accurate estimate of the prevalence of non- Lyme *Borrelia* in Australia is not possible. However, indirect estimates can be made based on TBD prevalence in Europe and the USA. In the Netherlands, Germany, Austria and the USA, the prevalence of TBD is 0.094%/year of the population (15). If we

extrapolate to Australia (population 25million), that translates to approximately 20,000 people/year incidence. The onset of symptoms can be delayed so that connection to the tick bite can be lost. This can create confusion leading to misdiagnosis. Therefore, many people can go on to become chronically ill with TBD and be misdiagnosed.

Clinical Significance/misdiagnosis: TBD have been known to mimic/contribute to the symptoms of many neurodegenerative diseases. This may potentially explain the high incidence of Australians suffering from chronic fatigue syndrome (CFS; 72,000 - 432,000)(20), Parkinson's disease (80,000, with a 17% increase in the last six years)(21), multiple sclerosis (MS; 23,700)(22), motor neurone disease (MND; 2000 with a 40% increase since 2000)(23) and dementia (380,000)(24). All of these diseases currently have no single identified cause and no cure, and 10% of incidences are attributed to genetics and 90% to environmental factors. Can tick pathogens contribute to the disease process? If these diseases had a purely genetic cause, the incidence would remain constant in the population

Burden of Disease on the health system and the Australian economy: Biggest burden of disease is created when acute form of TBD is misdiagnosed, allowing pathogens to disseminate creating multi systemic syndromic symptoms, a disease that is very difficult to treat with recovery being inversely proportional to the length of illness.

There are approved treatment protocols for the acute form of TBD from the Infectious Diseases Society of America (IDSA and Europe)(3). While, chronic TBD are complex to diagnose and to treat due to immune-dysregulation (38)and likely misdiagnosis and tissue damage. In developed countries, a large portion of the health budget is used for funding the ever-increasing number of chronic illnesses with poor outcomes for sufferers. There needs to be greater research investment into the cause of chronic diseases from the environmental, a multifactorial angle in order to reduce the burden on the health budget.

Chronic TBD can be misdiagnosed as one of a number of conditions, including: chronic fatigue syndrome [CFS]/myalgic encephalomyelitis [ME], multiple sclerosis [MS] (17), motor neurone disease [MND] (16), Parkinson's disease, and dementia (18,19). 90% of neurodegenerative diseases have an environmental cause and 10% have a genetic cause such as a mutation of a gene. As TBD can mimic the symptoms of neurodegenerative diseases, screening for TBD in patients suffering from neurodegenerative diseases and differential diagnosis should be encouraged. The cost of neurodegenerative diseases in Australia is listed below:

Cost of Neurodegenerative Diseases in Australia: CFS/ME \$525 Mil(20), Parkinson's \$7.6 Billion 1.7% increase last 6 years(21), MS \$2 Billion(22), MND \$500mil, 30% increase since 2000(23), dementia \$1.9Bil costing 1% of GDP by 2050(24). Total cost is over \$10 billion. A 30% increase in MND and 17% increase in Parkinson's disease suggest that environmental causes are contributing to the growth of these diseases in Australia. Ticks are considered the second most important vectors of zoonotic diseases after mosquitos. Yet understanding of ticks and tick pathogens is limited, especially their potential contribution to chronic neurodegenerative diseases. If the incidence of neurodegenerative disease were reduced by a mere 10% there would be a saving of over \$1 billion to the health care budget. If the savings for the social security budget is added, the total saving is even greater, probably 10 times more. •19.2%(2015-2016 budget)of the social security budget is spent on disabilities, that is 17.1 billion. 8.1 Billion on carers (1). There is a never ending demand. •Society cannot continue to fund these without increase in taxes and as the % of population working decreases there is an urgent need to research the environmental causes of these chronic diseases so preventative measures can be applied. Current treatment of Australian TBD is non-specific just as the symptomology. Overseas labs are used to diagnose and un-validated treatment protocols are employed because Australian health practitioners are not familiar and are not experienced in treating chronic TBD. People who recover do so from luck rather than science. Un-validated protocols advocated by alternative practitioners are applied without understanding the pathology of TBD clearly. These haphazard treatment protocols based upon popularity and not science inflate the cost of treating TBD in Australia. Therefore it is imperative that research into treatment is initiated in order to remove unnecessary treatment protocols and unnecessary costs to Australians suffering chronic TBD. In the USA the cost of treating TBD is \$712 mil to \$1.3billion, that is round \$3000 a patient(39). Similarly alternative treatment costs also add to the cost of treating chronic TBD in USA. Cost in Australia is likely to be more as there is greater use of alternatives and multiple health practitioner and hospital visits due to misdiagnosis and greater % are chronically ill. Burden on the individual: The tragedy of TBD is that sufferer's quality of life is very poor. Many are in chronic pain which even opioids do not alleviate, They have complex pathology ranging from clear physiological symptoms ranging from gut problems, tinnitus, to headaches, memory problems, seizures, fatigue, malaise, arthralgia, myalgia, flaccid paralysis, dyspnoea, tachycardia to bradycardia to dyspnoea, swallowing difficulties, allergies and more (38) Then there is the psychological symptoms including depression, mood changes, psychosis, volatile rages, communication and cognition problems and more. They cannot perform daily chores and look after their families. Usually families are so stressed due to the chronic illness and the stress of finding funds to pay for treatment protocols that relationships break up. People are desperate and want to get better. Hope of getting better drives them to explore and pay for un-validated treatments and keep trying treatment after treatment without a resolution. Those who can afford travel overseas to get treatment and some come back improved completely or partially. Getting better becomes an obsession with a high cost both emotionally and financially. What is the current research effort in TBD: Currently the only government funding for TBD research is held by Murdoch University through a Bayer grant of \$100,000/year for 3 years which is matched with an ARC grant. The research at the Tick Borne Diseases Unit, School of Medical Sciences, University of Sydney, is funded entirely by the Karl McManus Foundation. Murdoch Uni has ARC funding so TBDUnit, Uni off Sydney can should have NHMRC funding. So far there is no funding from NHMRC. The recent Senate Committee final report on Lyme-like illness in Australia (40) recommends research. Identifying pathogens in Australian ticks and other arthropods and characterizing them to determine their disease causing potential is needed. University of Sydney Tick borne diseases Unit, School of Medical Sciences, (Pharmacology) have identified different variants (from Murdoch) of relapsing fever Borrelia from Australian ticks. Establishing the disease causing ability in people: Currently Tick Borne Diseases Unit is screening people who are ill with tick borne diseases to identify the relapsing fever Borrelia that is infectious in people. Tick Borne Diseases Unit University of Sydney and Murdoch University are active in this area.

Designing better treatment protocols that is appropriate for Australian TBD: As per one of the Senate Committee recommendation 3.54 (40) The Karl McManus Foundation having funded research for 5 years and can see the huge impact of TBD on health and accordingly have taken the

significant step and commenced the process of forming the Karl McManus Institute (KMI) to expand the investigation of the multi-factorial causes of TBD. A funding process applicable to other research institutes like the Garvan Institute would expedite the applied research results to benefit all.

References:

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6. <https://qaafi.uq.edu.au/centre-for-animal-science>
7. Burgdorfer W. *Yale J Biol Med.* 1984 Jul-Aug;57(4):515-20.
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11. Russell RC, Doggett SL, et al. *Epidemiol Infect.* 1994 Apr;112(2):375-84

More references in next section

## Section 2

### The proposed TCR must have the potential to improve outcomes for the individual and/or community.

Give consideration to the following guidance questions:

How would a successful outcome of the proposed research affect the individual and community?

How would it reduce burden of disease for the individual and community;

Lower prevalence, and/or mortality, and/or morbidity;

Increased life expectancy or quality of life for those affected.

Would it improve prediction, and/or identification, and/or tracking, and/or prevention, and/or management within the disease area?

Is there a need for a community engagement plan to be requested of applicants for this TCR? If not, why is this not required?

Affect on community: Determination of human disease causing ability of Australian tick borne pathogens including relapsing fever *Borrelia* will help to alleviate controversy, bury the Lyme disease lexicon. It will enable the development of better diagnostics. People who are ill with TBD will be diagnosed and treated appropriately. It will reduce the very high incidence of misdiagnosis due to difficulty of clinical diagnosis. Most chronic diseases are descriptive without a cause or a cure. TBD, if diagnosed early are easily treatable. The current status of TBD in Australia is that most sufferers are chronic. The identification of tick borne pathogens and specific diagnostics for TBD will not only enable early diagnosis and treatment but also prevent the contribution of TBD to the pool of chronically ill people in Australia.

DALY/QALY, financial cost, lifestyle: In terms of DALY overall burden of disease is very high as people are so disabled they need carers and have been ill for 10, 20 year of their lives. Large portion of their lives are lost to chronic TBD. Many die from complications of chronic TBD such as multi organ failure. The stress affects their family and friends enormously. In terms of QALY burden is also very high in that daily they need a carer to perform personal care and household chores. If the cost of seeking medical advice from multiple health practitioners are added to the equation and acute hospitalizations due to seizures or other symptoms burden of disease is very high. It would be on par with the burden of caring for MS, MND and dementia sufferers. If the cost of TBD is added to the social security budget, the burden of disease skyrockets.

The burden of disease for the individual will be reduced significantly as the regained health means independence from carers and improvement of DALY and QALY. The individual would be able to be a positive contributor to society. Reducing the number of chronically ill will benefit the society at large, decrease the health care and the social security budget. Overall society will benefit from research into TBD. Research outcomes will reduce the mortality and morbidity of TBD sufferers and other diseases which TBD have been misdiagnosed as. Research outcomes that result in better diagnosis and treatment would help sufferers to regain their health which would improve their quality of life and life expectancy. Better identification and characterisation of tick borne pathogens would translate to better diagnostics better epidemiology, tracking and prevention. Community engagement would involve learning about dangers of tick bites and tick bite prevention methods which can be delivered via media. Funds would be needed to deliver the message to public about dangers of tick bites similar fashion to skin cancer.

People who suffer from TBD would not be the only people who would benefit from the research results. The sufferers have an opportunity to get diagnosis, treatment and recover from TBD to become positive contributors to society. DALY and QALY of TBD will be reduced very significantly. The health budget will have huge savings. Currently there are no legitimate studies of the savings of TBD treatment and patient recovery but over a 10 year period the savings to the health budget can be very large. Prevention of tick bites will help to prevent future infestations and create ongoing savings to the health budget.

Research Capacity and capability of the University of Sydney Tick Borne Diseases Lab is high with funding. The University of Sydney is of constructing medical premises to accommodate more medical research. The discipline of Pharmacology has labs in Charles Perkins Centre and the discipline can utilise the equipment and services of the Bosch Institute. Latest breakthrough for Australian TBD was the identification of relapsing fever *Borrelia* in Australian ticks by two labs. Successful outcome would give the sufferers their lives back. That is priceless. It would reduce the pool of people who are chronically ill and the burden of chronic diseases on the health and social security budget significantly. In addition the research would help to obtain epidemiology data and identify endemic TBD regions in Australia. Increased awareness improve prevention. and help to lower prevalence, mortality and morbidity.

In Australia TBD are under researched. In the past CSIRO was an active source of research into TBD albeit into animal husbandry along with the Dept. of Agriculture. Today most of the research facilities in Australia have closed except for the Tick Breeding Facility (6) outside Brisbane and a small lab at the University of QLD (5). As far as research into TBD and human impact is, even less researched and understood than animal research. In the early 1980's with the discovery of *B. burgdorferi sensu stricto* in the USA by Willy Burgdorfer (7) there were reports of cases of so called Lyme disease from the Hunter Valley(10) and from the South Coast of NSW (9). In 1989 an NHMRC grant awarded to Westmead Hospital to elucidate whether Lyme *Borrelia* is transmitted by Australian ticks (11).

TBD have been ignored by all, both by the research, and the medical community and the public at large for the last 21 years.

In 2010 with the passing of Karl McManus from complications of tick borne diseases, TBD started to come in to prominence by the public.

People with un-diagnosable illnesses began to identify with Lyme disease phenomenon from Dr Google and social media. Organisations like the Karl McManus Foundation begun to question the pathogens in Australian ticks causing infections other than *Rickettsia* going undetected leading to people becoming chronically ill.

It became evident that there was no ongoing research into TBD with *Borrelia* involvement in Australia.

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13. .Hudson BJ, Stewart M, et al. Med J Aust. 1998 May 18;168(10):500-2.
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15. Sykes RA, Makiello P. An estimate. J Public Health (Oxf). 2016
- 16 Harvey WT1, Martz D. Motor Neurone disease recovery. Acta Neurol Scand. 2007; 115(2):129-31
17. Brinar VV, Habek M.. MS. Clin Neurol Neurosurg. 2010 Sep;112(7):625-8
18. Cassarino DS, Quezado MM, et al Parkinsonism: Arch Pathol Lab Med. 2003 Sep;127(9):1204-6
19. Miklossy J. Alzheimer disease. Expert Rev Mol Med. 2011 Sep 20;13:

## Section 3

The proposed TCR must have the potential to reduce the burden of disease on the health system and Australian economy.

Give consideration to the following guidance questions:

- How would a successful outcome of the proposed research contribute to a sustainable health care system?
- How would it result in preventative health measures?
- How would it be translated into changes in policy?
- How would it reduce healthcare expenditure, and/or give greater value for given expenditure?
- What are the broader economic gains (e.g changes in workforce participation, a more educated workforce)?
- Does the proposed research have the potential to generate commercialised IP?

Contribution to sustainable healthcare?: Identification of pathogens in Australian ticks that are disease causing in people would help to differentially diagnose people who are infected with tick borne pathogens and treating those infected. This would help to reduce the number people who are ill in Australia. The overall health of Australians would improve. Although, currently the number of people who are ill with tick borne infections are not recordable the number could be as high as or higher than 0.094% of the population as is in the USA and Europe. Healthier Australians means huge savings in health dollars and increased productivity in Australians who would otherwise would be on welfare. Early diagnosis using improved diagnostics would mean early recovery. It would reduce the number who are chronically ill and save precious health expenditure.

Contribution to preventative health measures?: Research into tick borne pathogens, their identifications and characterization not only help in treatment but also in educating the public about dangers of tick bites. Knowledge about tick borne pathogens can be transferred into tick bite prevention measures which would be communicated to the public and health practitioners. Thereby if anyone is bitten they would seek medical advice urgently. Currently, Karl McManus Foundation (14) is trying to educate the public about the dangers of tick bites. Decreased number of tick bites would result in decreased number of ill people. Changes in policy: Policy change would involve focused research funding for tick borne pathogens and tick borne infections being treated seriously. Adopting the Senate Committee report recommendations would help all stakeholders. Better education of health practitioners would help to improve diagnosis rates, enable differential diagnosis. Better education of the public about the dangers of tick bites would increase positive outcomes, reduce healthcare expenditure?: Identification and characterization of tick borne pathogens would result in appropriate diagnosis and treatment which would help to reduce health care expenditure. In that currently many patients who are ill with tick borne pathogens are being misdiagnosed. Misdiagnosis is due to unfamiliarity of health care practitioners with the signs and symptoms of tick borne infections, unreliable diagnostics coupled with non-specific and multi-systemic nature of symptoms. Improved diagnostics means better identification of infected people and treatment and decreased number of people who are chronically ill. And decrease in the number of people entering the chronically ill pool, is a huge saving in health and social security dollars. Economic gains: Best economic gain is healthy citizens which translates to increased productivity as a nation and improvements in standard of living. This research would even benefit other nations globally.

IP Potential?: The diagnostic tests developed have potential to generate IP. In addition new treatment protocols also have potential to generate IP. The benefit of increasing the number of people off welfare and back in the workforce would be boundless.

References Continued:

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## Section 4

The proposed TCR will contribute to the global research effort.

Give consideration to the following guidance questions:

- Is the issue of global significance?
- How would the proposed research contribute to international research efforts?
- What original contribution would this research make?
- Is it building upon previous research, or linking with research on the same issue?

Is the issue of global significance?

TBD were investigated by WHO before the advent of AIDS. But post AIDS funding for TBD were channeled into prevention and treatment of AIDS. So for over 30 years TBD have been neglected globally. In the USA since 1990's there has been an ongoing focus on debate about the existence of chronic Lyme disease. The political debate has contributed to the lack of significant advancement in TBD. The focus on Lyme disease has also prevented the research into non-Lyme Borrelia infections and other pathogens that are transmitted by ticks. e.g: Babesia, Bartonella. The discovery of relapsing fever Borrelia in Australia, where previously was thought that there is no Lyme Borrelia re directs Australian research away from Lyme disease. How Australian relapsing fever Borrelia (34) contributes to symptoms of TBD can help to reduce the USA controversy as some people with chronic Lyme disease may have relapsing fever aberrants, like B. miyamotoi (35,36) and for which treatment protocols can be developed and validated.

How would the proposed research contribute to international research efforts?

Research into relapsing fever and other tick borne pathogens in Australia would significantly increase the global understanding of these types of pathogens and infections they cause.

Currently World Health Organisation has two different ICD codes one for Lyme disease and one for relapsing fever and infections by B.miyamotoi or other aberrant Borrelia have not been accounted for. In addition immune dysfunction that occurs when tick borne infections are not diagnosed early have not been considered.

There is a void in understanding of environmental factors that contribute to chronic diseases. Tick borne diseases with non-specific symptoms are easily misdiagnosed and can contribute to the pool of chronic diseases that is a currently a huge burden for developed countries and developing countries are catching up rapidly. There are global awakening about tick borne diseases, albeit it comes as a Lyme disease movement which muddies the communication channels between all stake holders. and makes it difficult to move forward by all parties.

Original contribution would this research make?: This research project would contribute to better understanding of TBD in Australia and globally. Currently it is accepted that tick bites in Australia can make people ill and produce symptoms like Lyme disease in the USA. But the causative agent has not been identified yet. This research project would solve this mystery. Australian Borrelia has been found to be a unique clade which can provide unique insight in the mechanism of bacterial heterogeneity and the disease process. With >21 plasmids Borrelia (29) is a rare bacterium and pathology it creates in the host is also unusual. A paradigm shift is needed in the way bacterial infections are viewed. If Staphylococcus aureus with one plasmid can cause so much havoc in the health system imagine the power of > 21 plasmids can do if we ignore infections caused by Borrelia globally.

Is it building upon previous research, or linking with research on the same issue?

TBD research have been neglected in Australia for over 20 years. Recently 2 (East Coast and West Australia) labs have found relapsing fever Borrelia in Australian ticks (34). These relapsing fever Borrelia are genetically different from each other which suggest there are so many other variants of Borrelia in Australia. Similar assumption can be made for other pathogens such as Babesia, Bartonella Ehrlichia vectored by ticks or other arthropods in Australia. The current research projects would bridge that gap and increase our understanding of TBD and their impact on human diseases not only in Australia but globally . Relapsing fever Borrelia infection is endemic in Africa, Asia and Middle East, in developing countries where research funding is very limited. Australian relapsing fever research would help the developing countries in diagnosing and treating relapsing fever. In Africa it is common to misdiagnose relapsing fever as malaria. So what % of 300 million people who have malaria also have relapsing fever?. Furthermore Australians traveling to the endemic countries would also have a better chance of getting appropriate diagnosis. Between 2014-2015 9 million Australians traveled overseas, significant number to Asia and Africa. 0.094% infestation with TBD would translate to over 8000 people being infected. If not diagnosed early because of lack of understanding of relapsing fever most of these people would become chronically ill. If each year 8000 people were added to the chronically ill pool for the next 5 years would translate to 40,000 being added to the chronically ill pool. This number excludes people bitten in Australia. These numbers clear indicate that there is an urgent need to fund research into relapsing fever Borrelia infection not only in Australia but globally.

## Section 5

Please enter any additional information relevant to your proposal that does not fit in with the above questions.

Environmental conditions that encourages infections: Climate Change

There are also other factors that help in the spread and distribution of TBD. Arthropods feeding on reservoir animals travel to different areas for food and shelter. Therefore changes in climate which result in variations in availability of food for the reservoir animals and their ticks can also change the demographics of TBD not only in Australia but also globally. Hence TBD can occur in non-coastal areas. In addition, shallow feeders also fly to feed on inland lakes, therefore the spread of ticks/arthropods and TBD in those areas of inland water ways can increase correspondingly.

In hot tropical climates where temperatures can remain optimal for tick or other arthropod reproduction (27-28degrees Celsius) throughout the year instead of being seasonal as is in the Northern hemisphere, can result in high arthropod numbers and can reach high densities(28). High

populations of arthropods mean a high incidence of human contact by vectors and therefore a high incidence of TBDs. So, is climate change affecting arthropod demographics? A study in the USA found an increase of 2°C degrees increase in mean temperature can increase the virulence of Borrelia in the MidWest of the USA(30).

Source of infection to be confirmed: Migratory Birds: The geographic distribution of TBD is hard to locate accurately because of the difficulty in diagnosis and the delayed onset of symptoms. However, ticks are vectors, like other arthropods, and their main form of transport round the globe is via birds. Therefore the demographics of TBD can be linked to areas where bird migrations take place. For example, the areas under the Australasian flight path of coastal birds (shallow feeders) can have a high incidence of TBD as ticks are carried by birds which feed on local fauna, which then can become reservoir animals that can continue to spread the pathogens via local arthropod vectors. This was suggested by a study by Professor Richard Barry of the University of Newcastle in the 1990s(12) which found a high incidence of Borrelia infection in the northern beaches of Sydney and other coastal areas in northern NSW. From this information we can surmise that coastal areas in Australia are likely to have a high incidence of TBD, but more studies in demographics need to be done to obtain more reliable statistics.

Tick borne infections can challenge our current microbiological principles. In that TB pathogens do not replicate rapidly and have rapid onset of symptoms e.g: E.coli, 20minutes, while Borrelia 24 hr, so there is delayed onset (can be months, years) of symptoms. Our medical system is capable of treating mono-pathogenic infections with one antimicrobial magic bullet. TBD in contrast are usually multi-pathogenic, the number and type delivered can depend on the previous host of the tick. So there is high heterogeneity in tick borne pathogens. It is difficult to define a disease when there are multiple pathogens involved and symptoms are non-specific and multi-sytemic. TBD would have difficulty in fulfilling the Koch postulates.It is difficult to decipher which TBD symptom belong to which pathogen and how do each pathogen interact with each other and the host. As for treatment which pathogen do you treat first? How do you prevent Herxheimer reaction? If TBD pathogens have disseminated how do you kill the pathogens, prevent Herxheimer reaction and tissue damage?

Is my proposal completed and ready to be submitted?:

Yes, my proposal is completed and ready to be submitted