



IUSTI Asia Pacific Sexual Health Congress 2018

The roles of mast cells and their proteases during *Chlamydia* infection

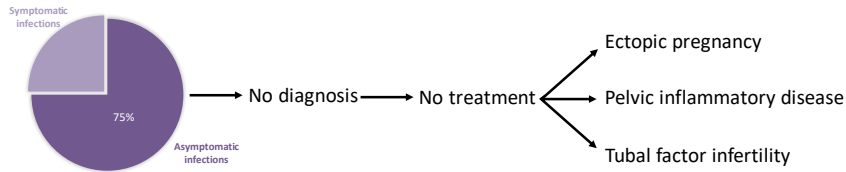
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Disclosure: No potential conflict of interest

131 million cases of *Chlamydia* infection every year

- Young and indigenous populations → higher rate of *Chlamydia* infection



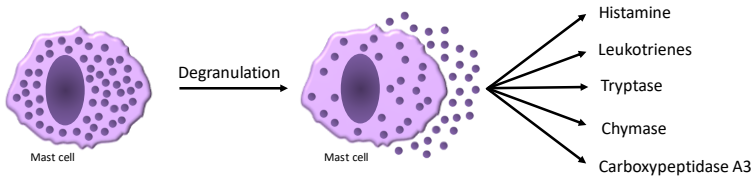
A better understanding of the immune responses to *Chlamydia* infection is required
→ Mast cells represent a novel target



WHO, Sexually transmitted infections, 2016
Haggerty et al., J Infect Dis, 2010
Debutista et al., Fertil Steril, 2009
The Kirby Institute, HIV, viral hepatitis and sexually transmissible infections in Australia Annual Surveillance Report, 2015
WHO, Global prevalence and incidence of selected curable sexually transmitted infections: Overview and estimates, 2001

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NSW Health
Hunter New England Local Health District

Mast cells are large granular immune cells

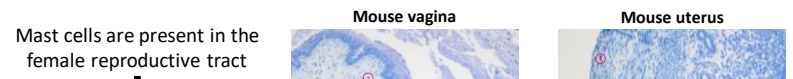


Mast cells play an important role in *Chlamydia pneumoniae* lung infection by facilitating immune cell recruitment into the airway (Chiba et al., *J Immunol*, 2015)

↓

Tissue damages

Mast cells are widespread in the female reproductive tract



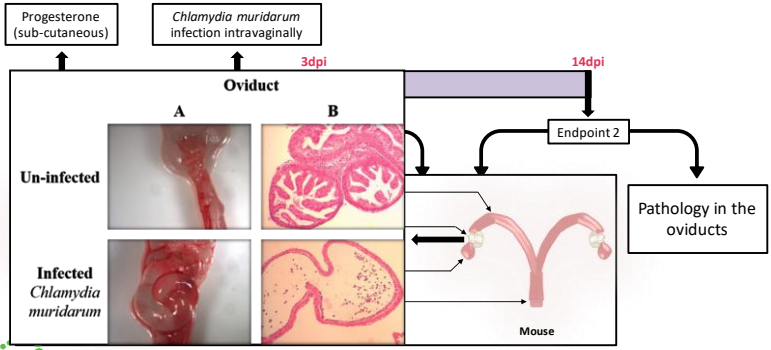
Hypothesis

Mast cells and their proteases play an important role in regulating immunity to *Chlamydia* infection and associated pathology in the female reproductive tract

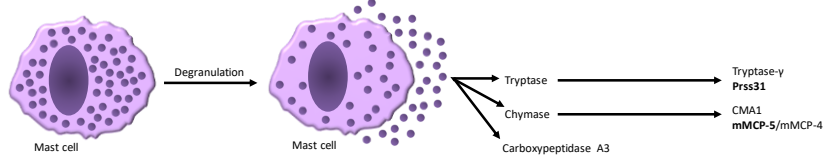
Protection against Group B *Streptococcus* infection

Toluidine blue staining
 Purple = mast cells / Blue = tissue

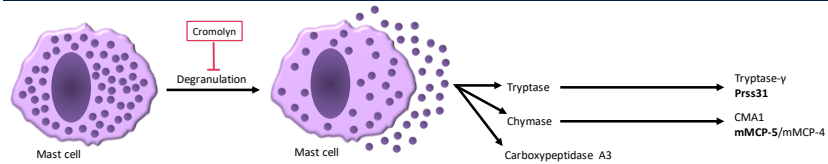
Murine model of *Chlamydia* infection



Targeting mast cells experimentally

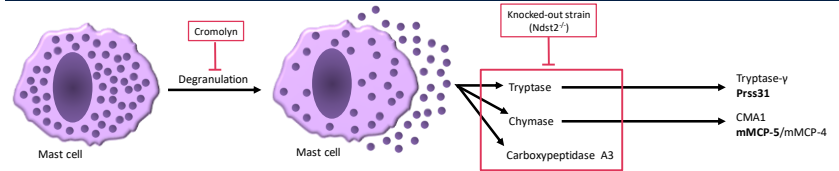


Targeting mast cells experimentally



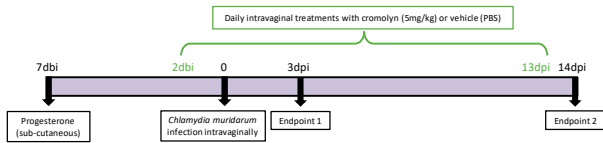
Mouse line	Genetic modification	Treatment
WT	-	Cromolyn Inhibitor of degranulation

Targeting mast cells experimentally

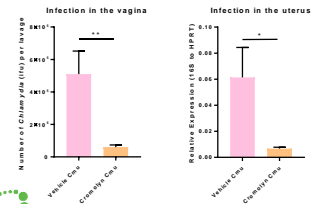
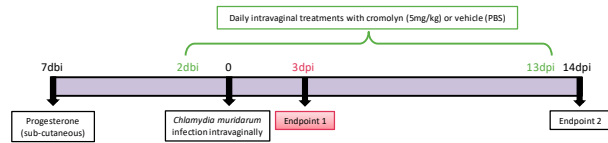


Mouse line	Genetic modification	Treatment
WT	-	Cromolyn Inhibitor of degranulation
Ndst2 ^{-/-}	Deficient in N-deacetylase/N-sulfotransferase 2 → Altered protease storage in granules	-

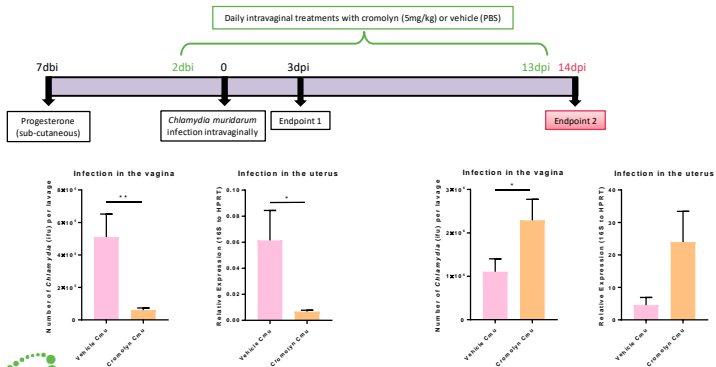
Cromolyn treatments are protective against early infection



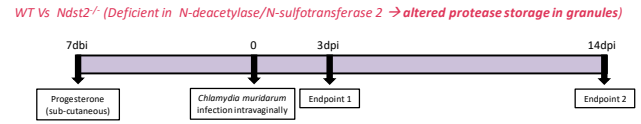
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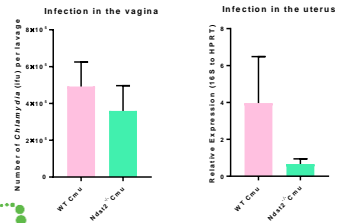
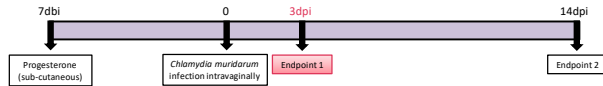
Ndst2 deficiency protects against *Chlamydia*-associated pathology



HMRI logo and institutional affiliations: University of Newcastle, Health Research Centre, NSW Health, Hunter New England Local Health District.

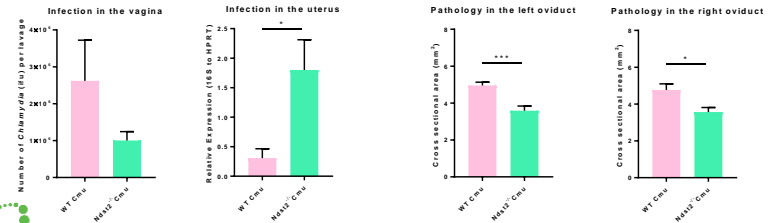
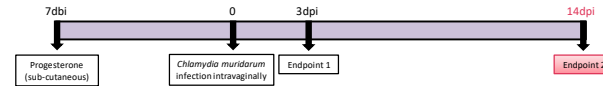
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WT Vs *Ndst2*^{-/-} (Deficient in *N*-deacetylase/*N*-sulfotransferase 2 → altered protease storage in granules)

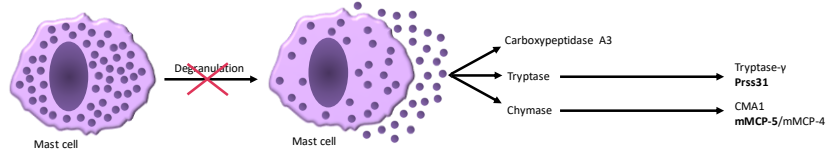


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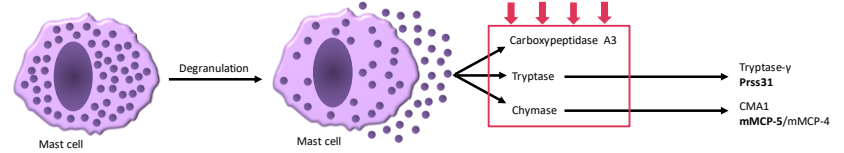


Mast cells and their proteases affect *Chlamydia* infection



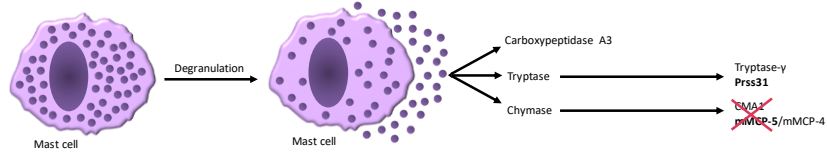
Mast cell and proteases	3dpi		14dpi	
	Infection	Infection	Pathology	
Cromolyn	Protective	Detrimental	No effect	

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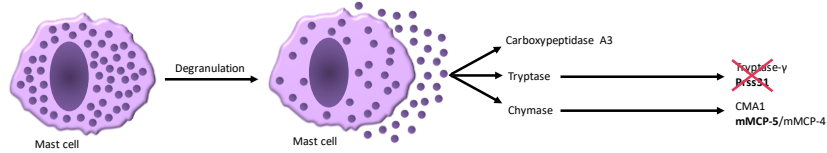
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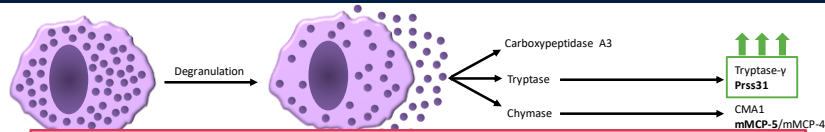
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Mast cells and their proteases affect *Chlamydia* infection



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	3dpi	Infection	Pathology
Cromolyn	Protective	Detrimental	No effect
Ndst2 deficiency	No effect	Detrimental	Protective
mMCP5 deficiency	Protective	No effect	No effect
Prss31 deficiency	Detrimental	Detrimental	No effect

Mast cells and their proteases affect *Chlamydia* infection



Many proteases make up one mast cell

He muka nō taura whiri - Many strands make up one rope

Ndst2 deficiency	No effect	Detrimental	Protective
mMCP5 deficiency	Protective	No effect	No effect
Prss31 deficiency	Detrimental	Detrimental	No effect
rPrss31 treatment	Protective	No effect	Protective

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Acknowledgements



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Lab colleagues:

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- Dr. Andrew DEANE
- Dr. Richard KIM
- and all others

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