



Urinary Stones in Bichons: Using research to crack the code

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Resources

- **Minnesota Urolith Center** – urolithcenter.org
 - MN Urolith App to predict stone type
 - Android/Google Play
https://play.google.com/store/apps/details?id=com.hawthornemackenzie.crowell256aa.mn_urolith
 - Apple/App Store <https://apps.apple.com/us/app/mn-urolith/id1035128900>
 - This app has two functions to predict stone type that do not require an account – **CALCulate** and **CALCurad**
- **UMN Canine Genetics Lab** – z.umn.edu/caninegenetics
 - CaOx research page – z.umn.edu/stones

Disclosures

I am a member of the [UMN Canine Genetics Laboratory](#) which offers genetic testing for stone risk mutations; proceeds support further research

I am the co-director of the [Minnesota Urolith Center \(MUC\)](#), which is supported by pet owners, veterinary clinics, and an educational gift from Hill's Pet Nutrition



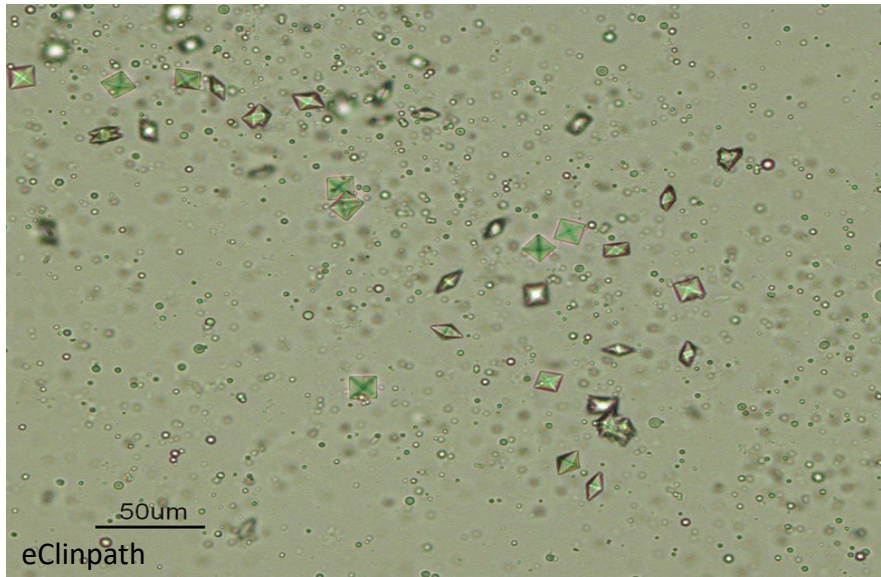
The Minnesota Urolith Center receives greater than **60,000 urinary stone** submissions from dogs each year



Bichons Frise are at increased risk for urinary stones



Urinary stones form when dissolved substances in the urine form crystals which cluster and grow into a solid mass



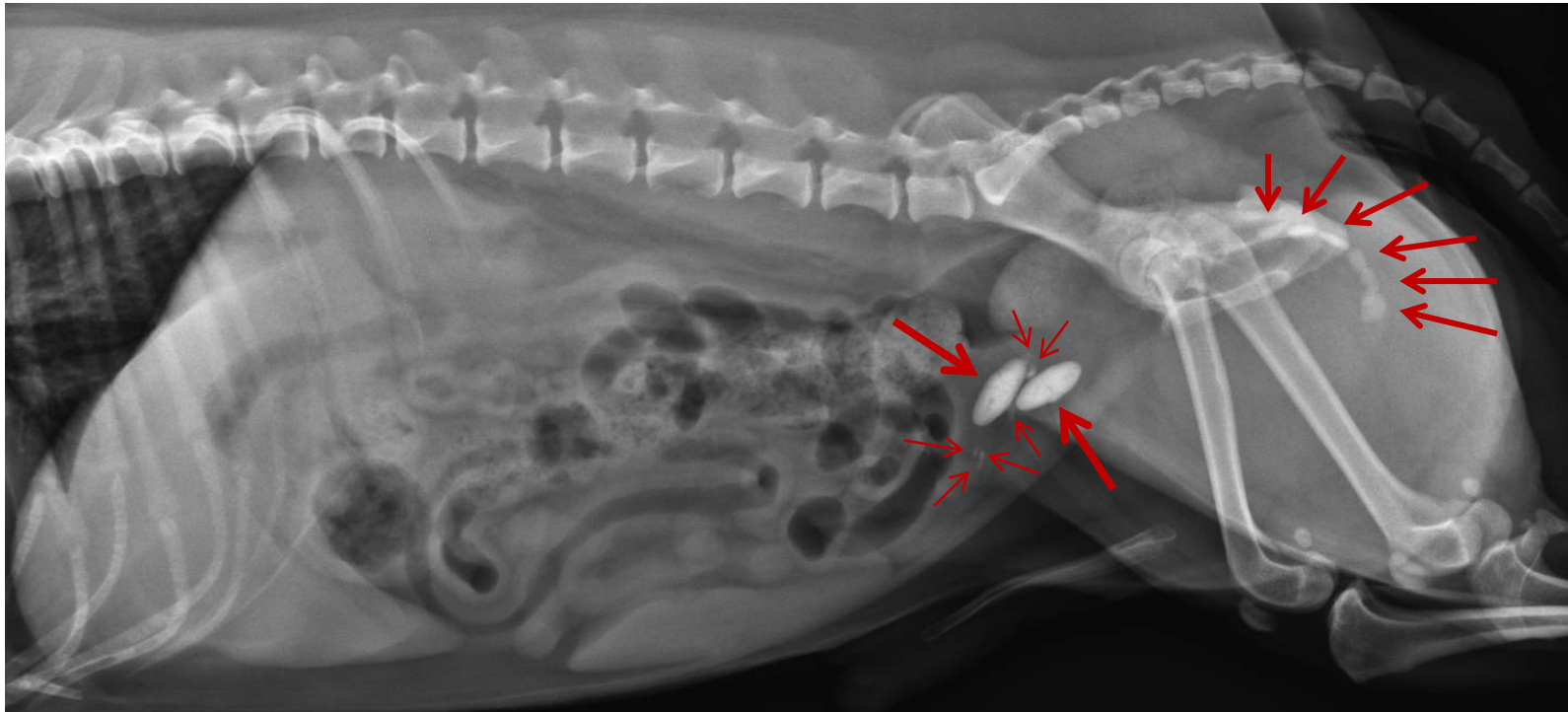
Urinary stones can be very painful

Signs include frequency, urgency, blood, and straining with urination



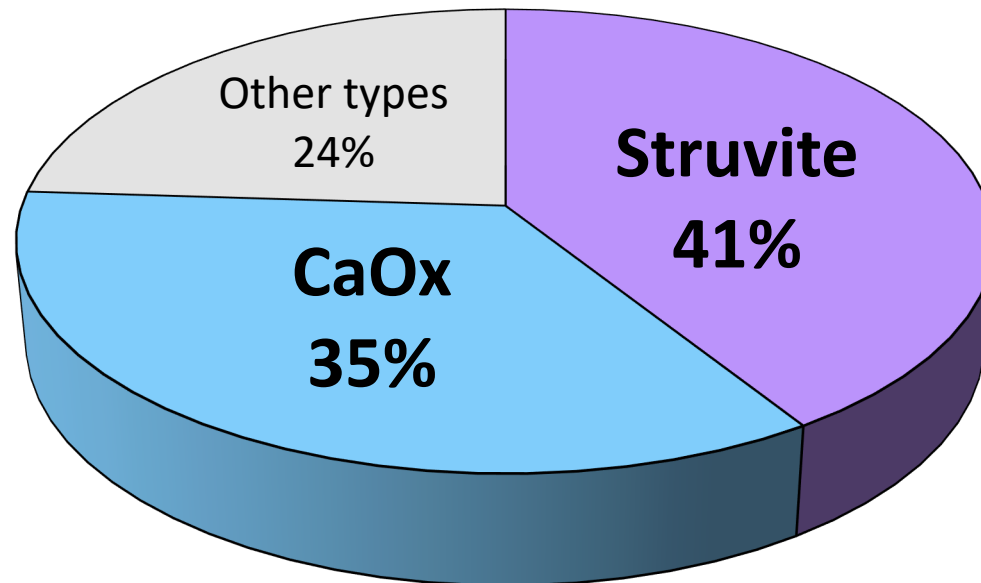
Urinary stones can be very painful

Life-threatening obstructions can occur



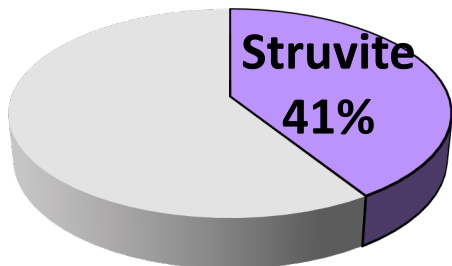
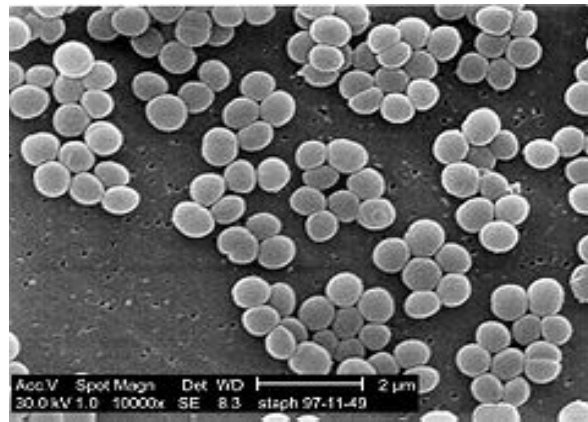
There are two main stone types, which have different causes

Bichons are high risk for both

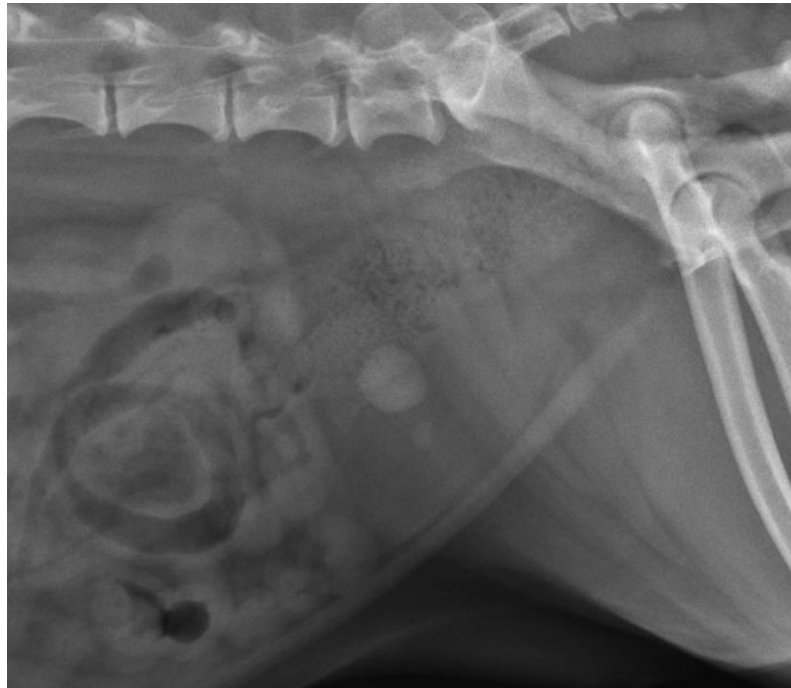
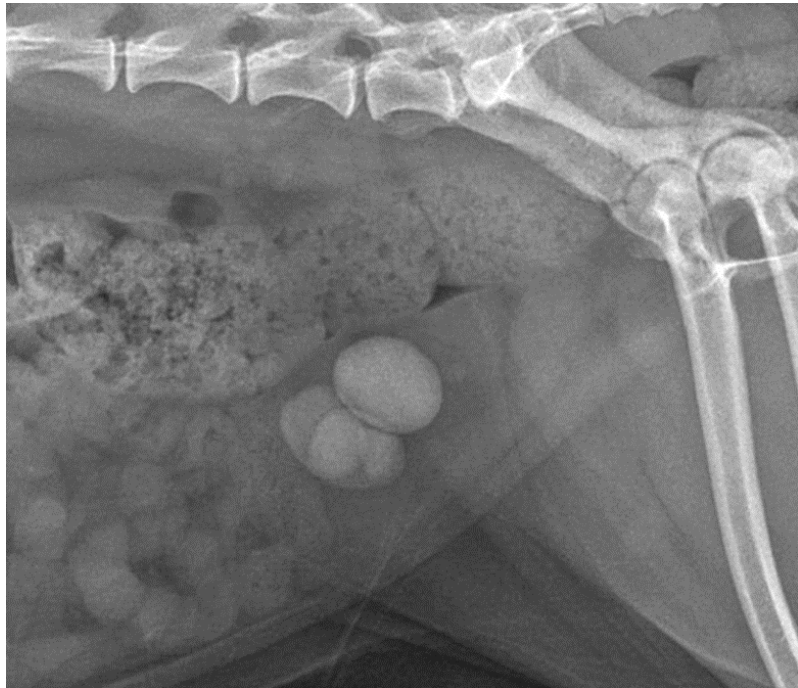


In female dogs, most stones are composed of struvite

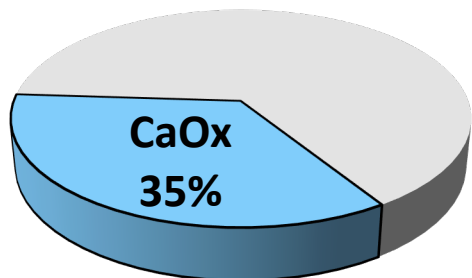
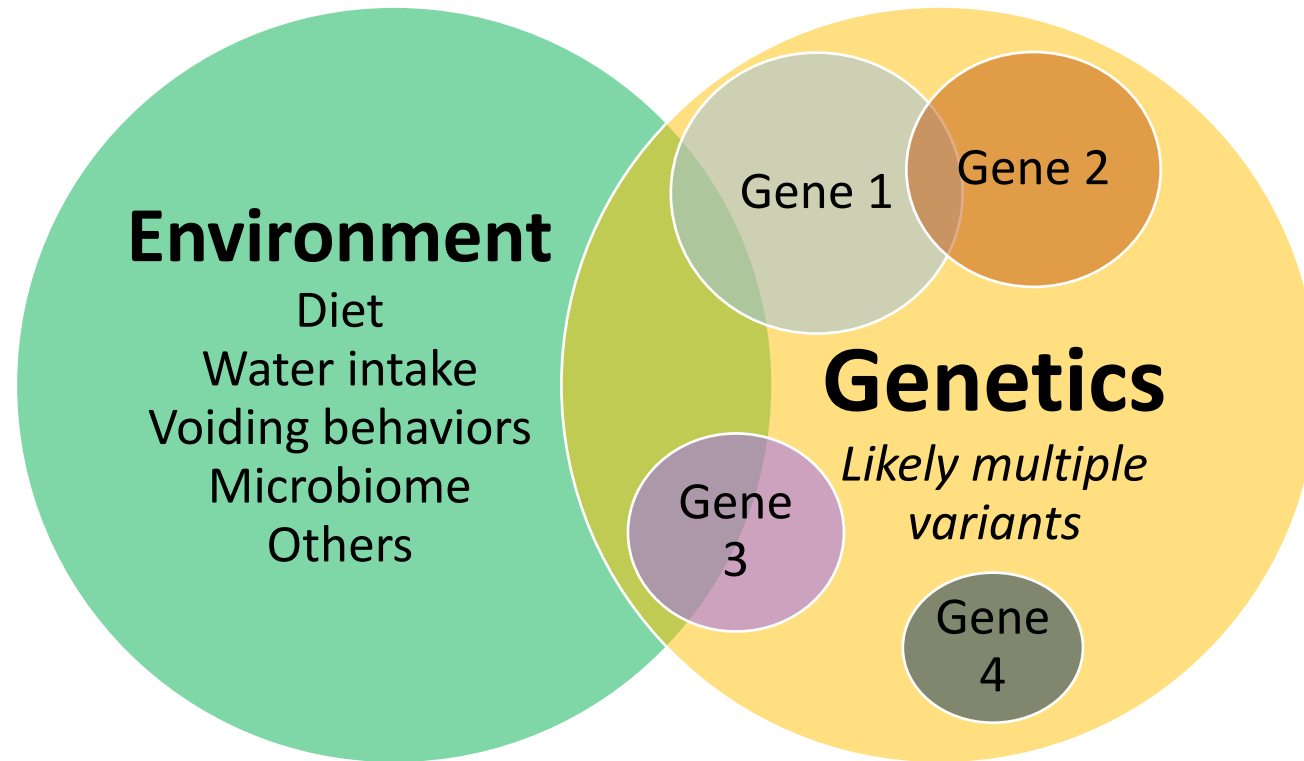
This stone type is caused by a urinary tract infection



Struvite stones DISSOLVE with a therapeutic diet and antibiotics



In male dogs, most stones are composed of calcium oxalate
The cause of this stone type is complex and poorly understood



CaOx stones do not dissolve

Stone removal is required for dogs with signs of discomfort



<http://drstephenbirchard.blogspot.com/2014/10/cystotomy-for-removal-of-cystic-and.html>

CaOx stones do not dissolve

Stone removal is required for dogs with signs of discomfort



CaOx stones are highly recurrent
1 in 2 dogs have a recurrence
within 2 years



**My goal is to discover causes of
CaOx stones in order to better
prevent them, thereby reducing
pain and suffering**



**Which is the driver of CaOx stones in Bichons –
calcium, oxalate, or both?**

[Ca²⁺]



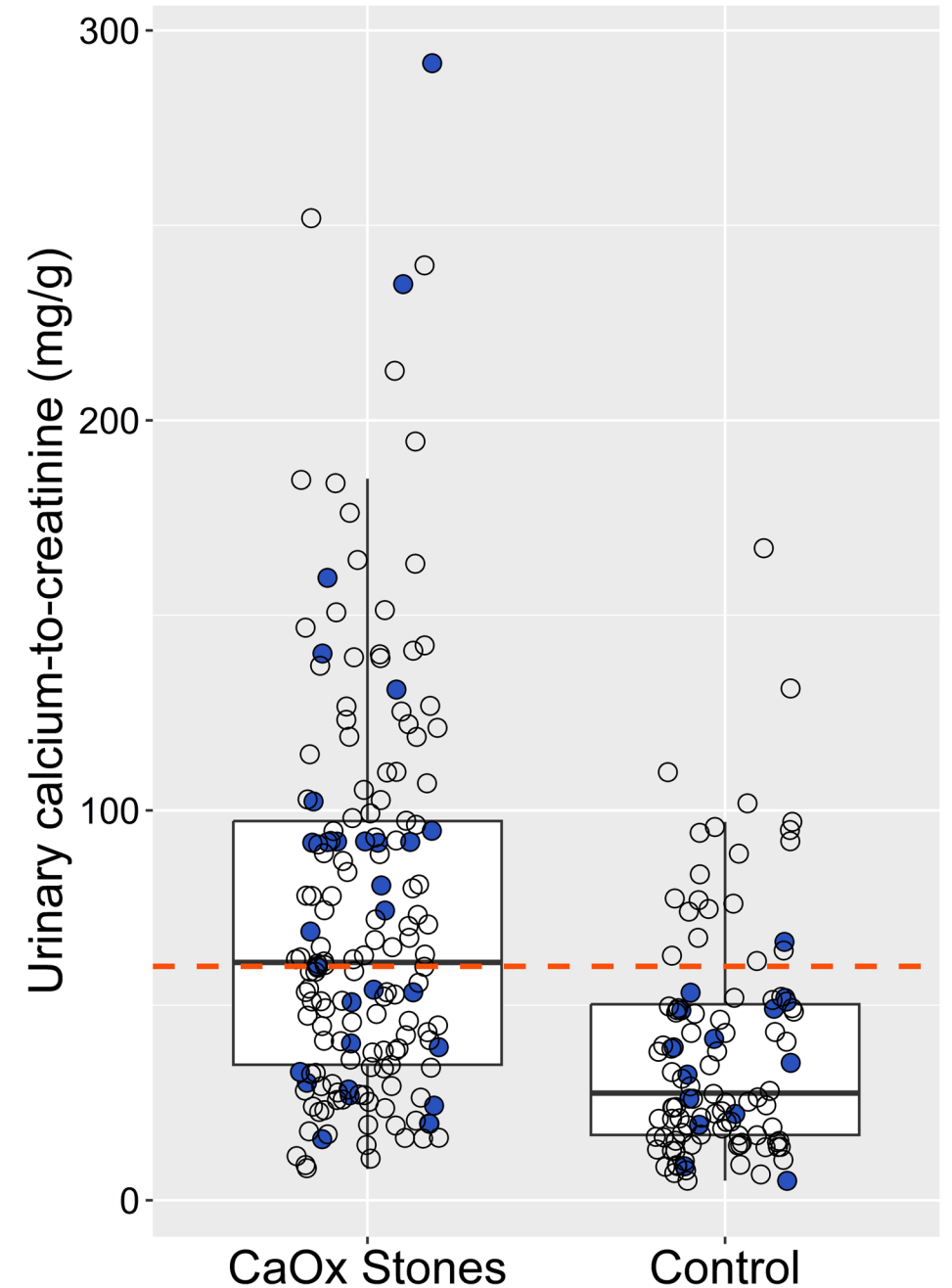
[Ox²⁻]

Discovery 1

**Most Bichons with CaOx stones have
high urinary calcium, much like human
stone formers**

“Hypercalciuria”

[Ca²⁺]

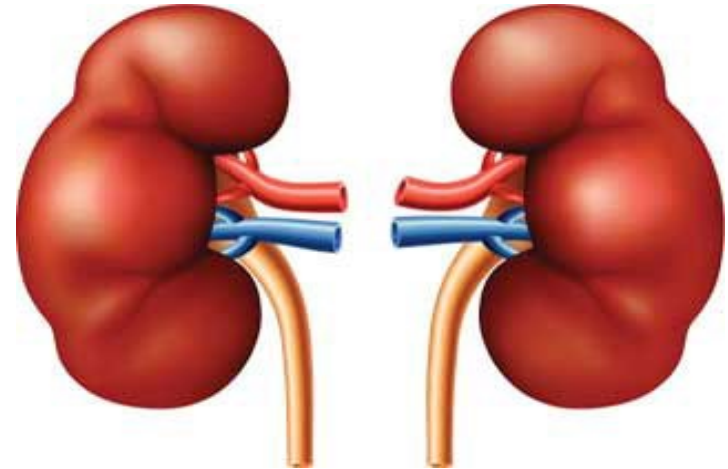


Discovery 1 - Impact

We can diagnose hypercalciuria and directly treat it with medication



Reduces calcium
excretion into urine →

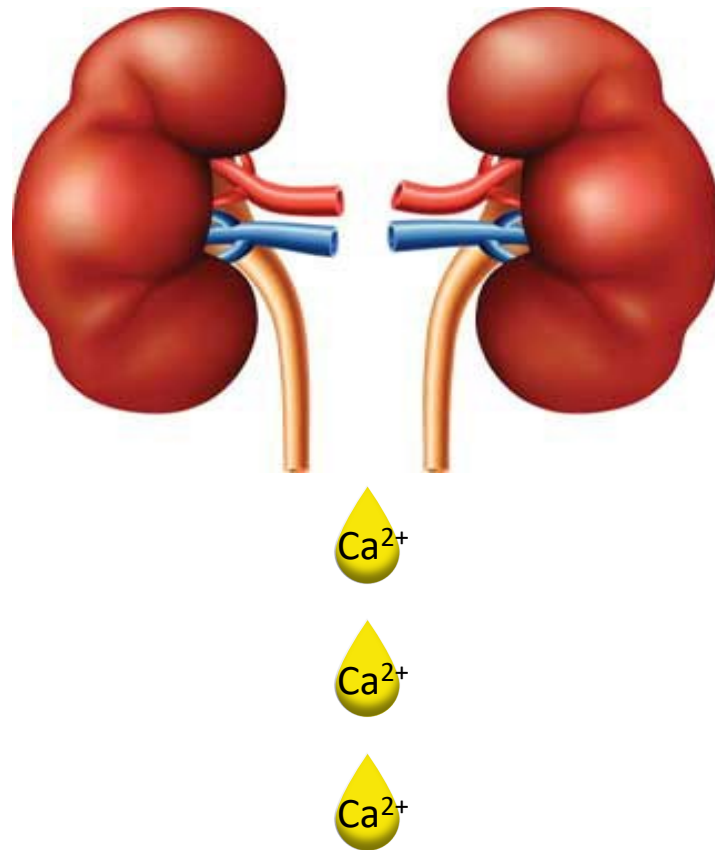


Discovery 1 - Impact

Increasing water intake also reduces urinary calcium concentrations

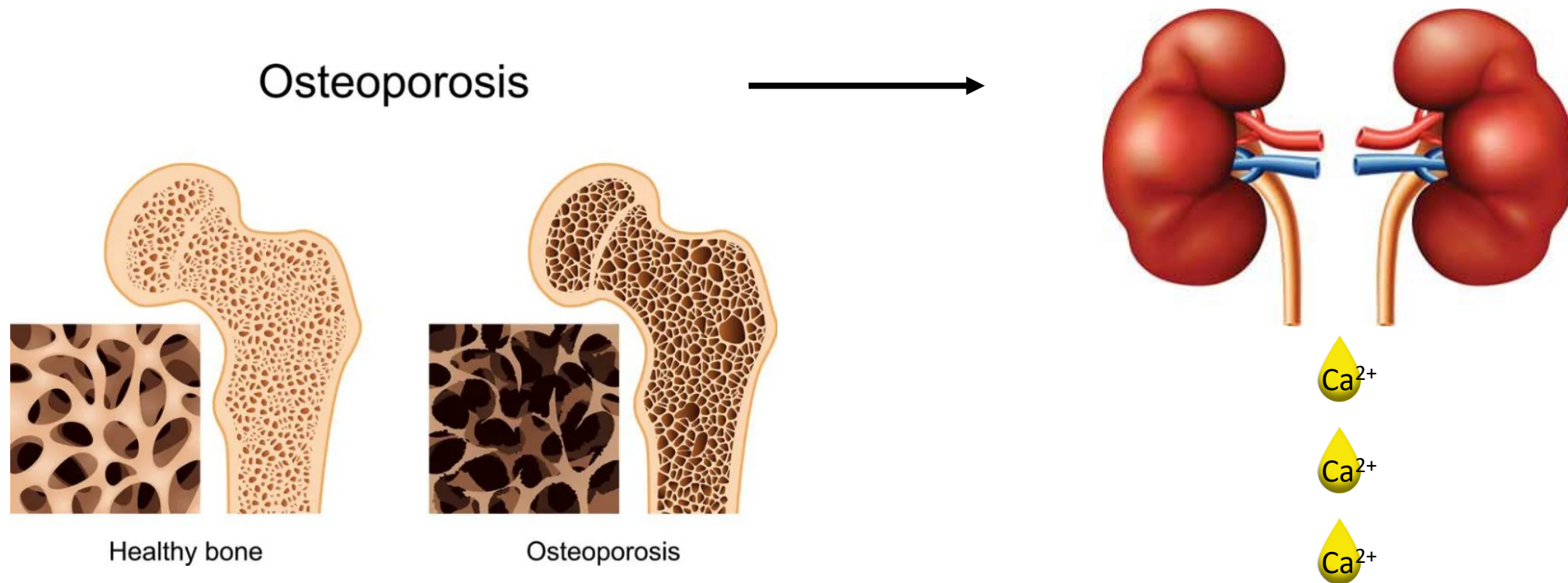


Where does the excessive calcium come from?



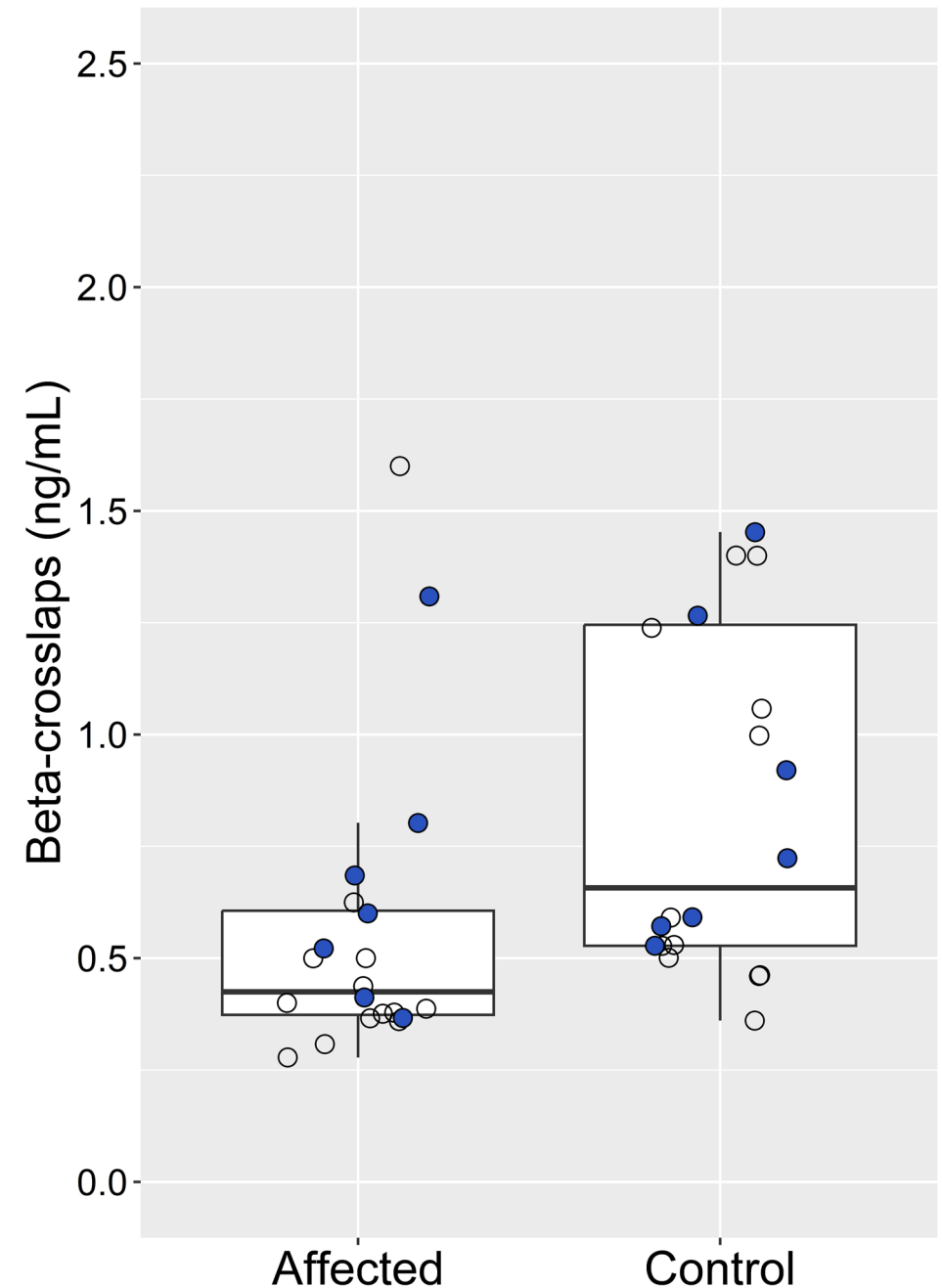
One source of high urinary calcium excretion is bone turnover

This is common in human kidney stone formers



Discovery 2

Bichons with CaOx stones have normal to low bone turnover, which means bones are NOT the source of hypercalciuria



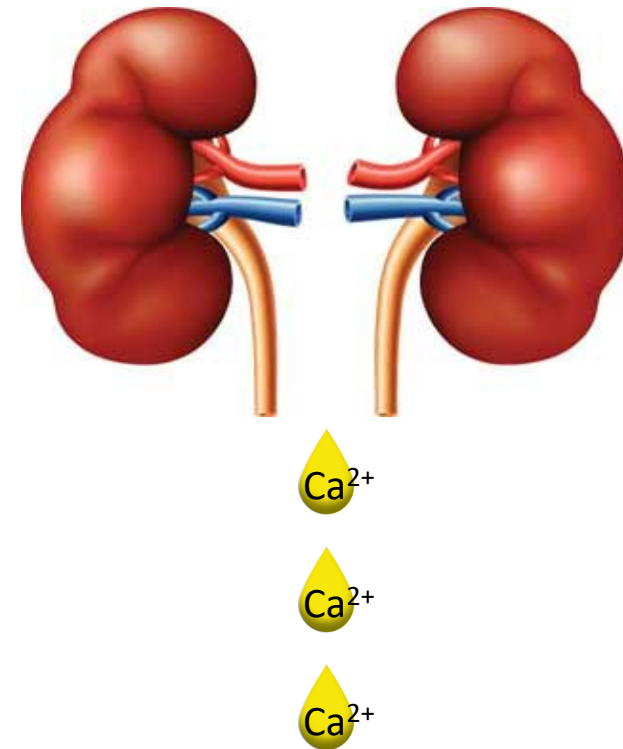
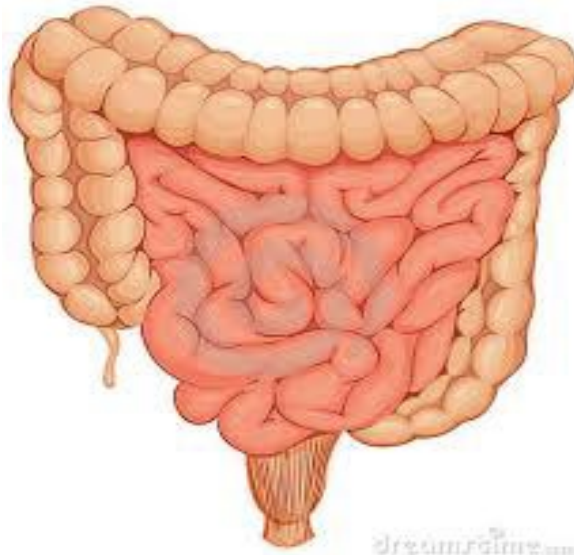
Discovery 2 - Impact

There is no indication to treat stone-forming Bichons Frise with drugs to reduce bone turnover, and it might be dangerous to do so



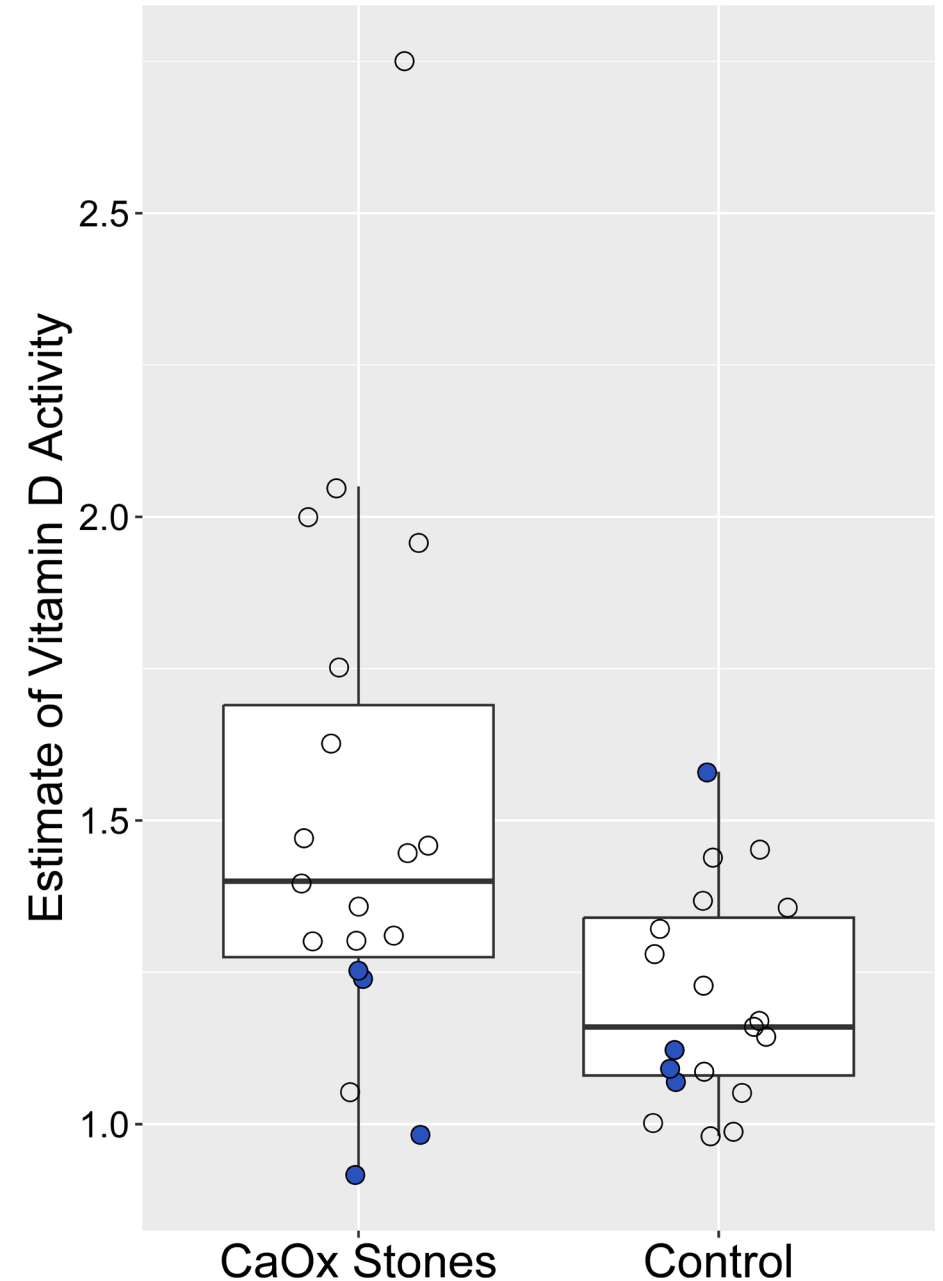
Another source of high urinary calcium excretion is the gut

Vitamin D is a major regulator of intestinal calcium uptake



Discovery 3

Increased vitamin D activity might be a source of increased gut calcium absorption in some dogs with CaOx, though not yet identified in Bichons



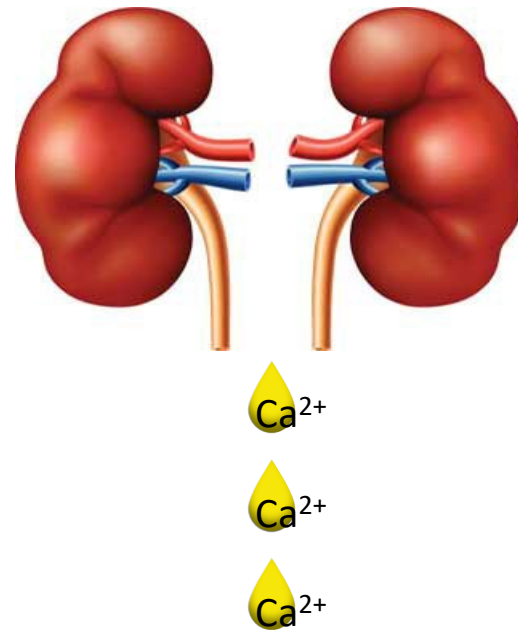
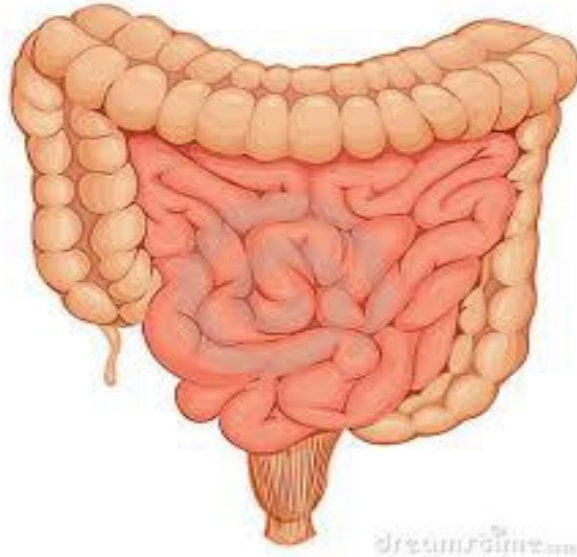
Discovery 3 - Impact

Supplements containing vitamin D should be avoided for dogs with CaOx stones



The source of excessive urinary calcium in Bichons with stones is currently unresolved and is likely not the same for all dogs

Gut? Kidney? Both?



**Urinary calcium is generally high in Bichons with CaOx stones
but what about oxalate?**

$[\text{Ca}^{2+}]$

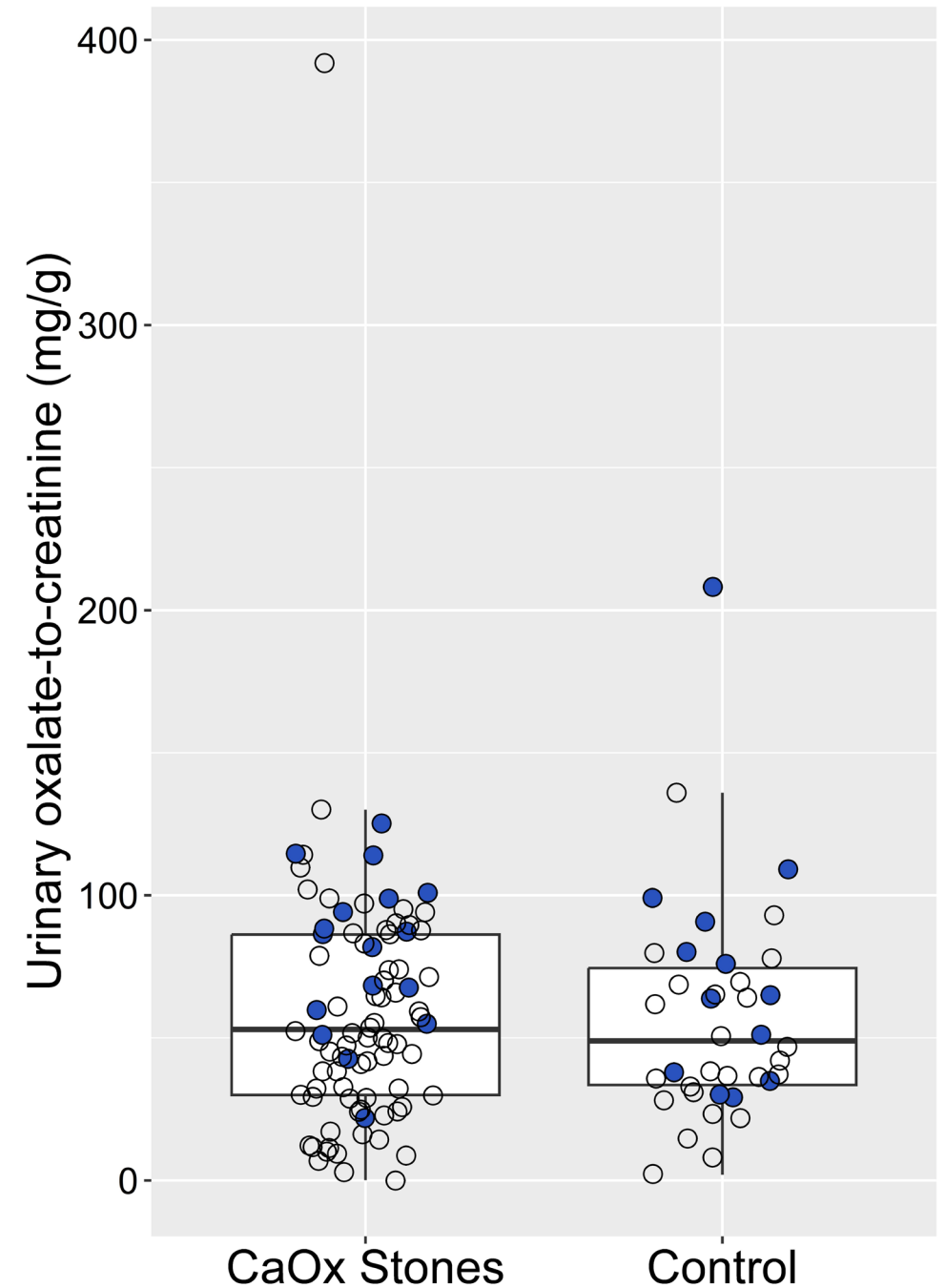
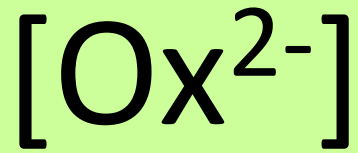


$[\text{Ox}^{2-}]$



Discovery 4

Urinary oxalate is **NORMAL** in
Bichons Frise with CaOx stones



Discovery 4 - Impact

Treatments to alter oxalate metabolism are unlikely to help, as this pathway does not appear abnormal



No benefit?

However, reducing dietary oxalate benefits CaOx stone formers in general

Oxalate content of dog food is not reported on labels and many “healthy” ingredients are high oxalate

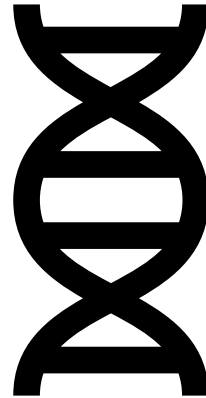
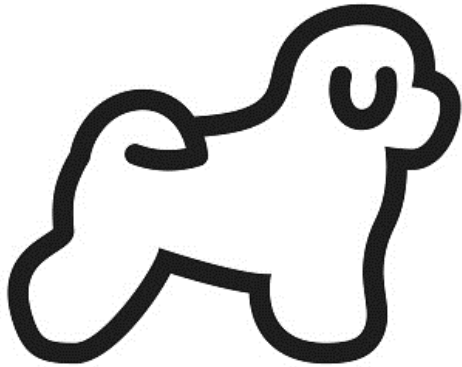


There are therapeutic urinary diets formulated to minimize oxalate

For human foods, there are online resources with oxalate information

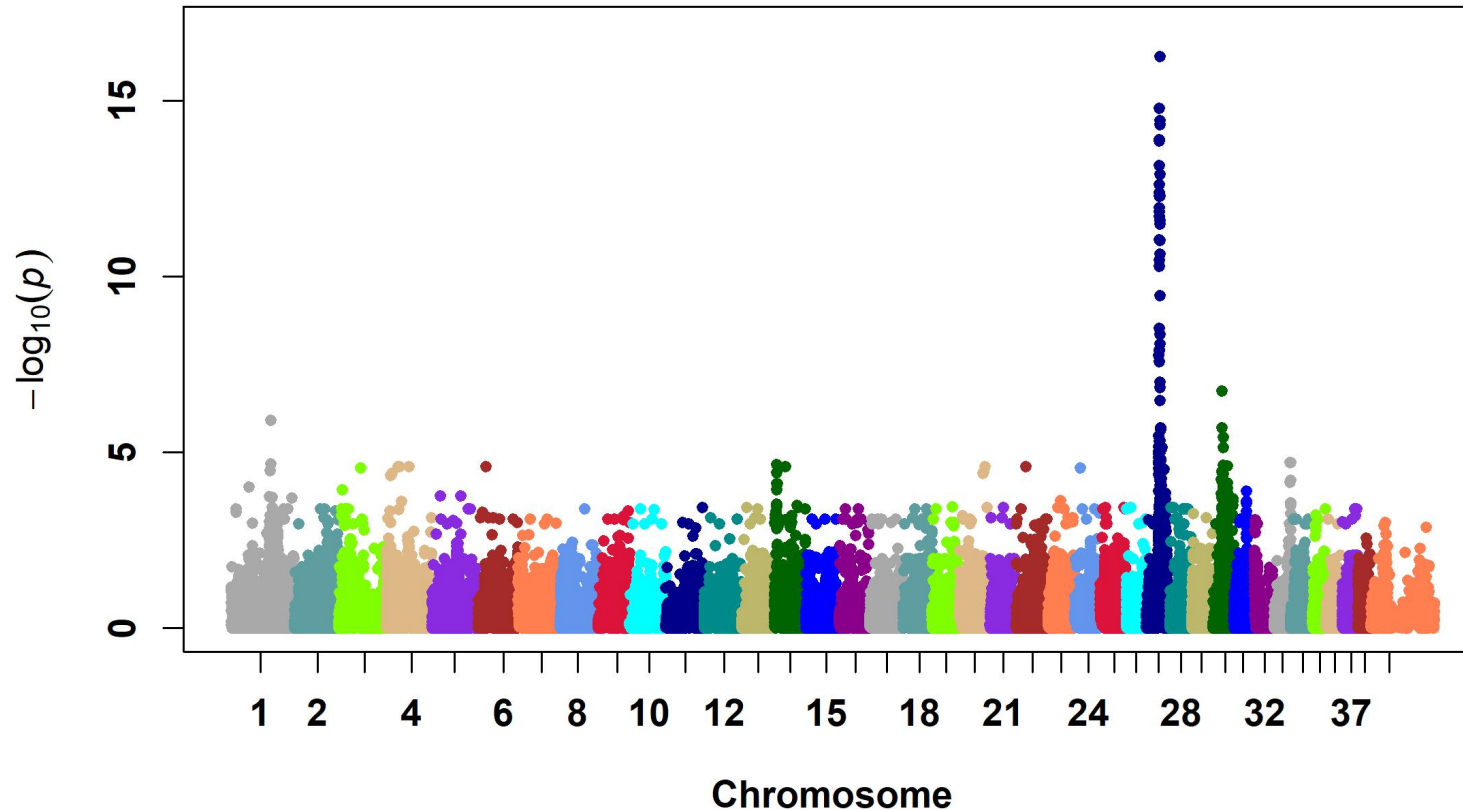


**Are there genetic risk factors we can identify and target to prevent
CaOx stones in Bichons?**



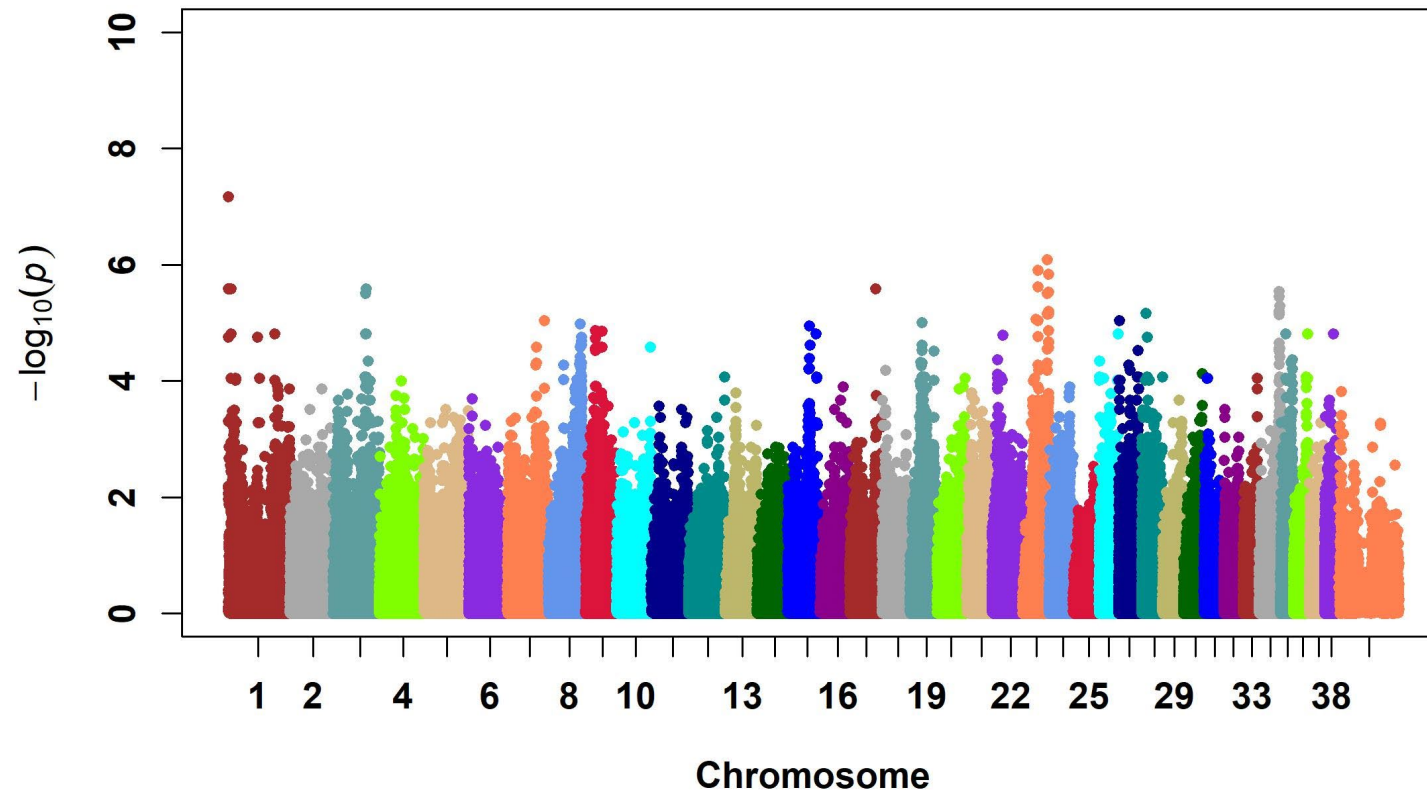
Genome-wide association studies are one approach to identify the location of genetic risk factors

Example discovery of a cause of cardiac disease in Manchester Terriers with a peak on the chromosome where the responsible mutation was located

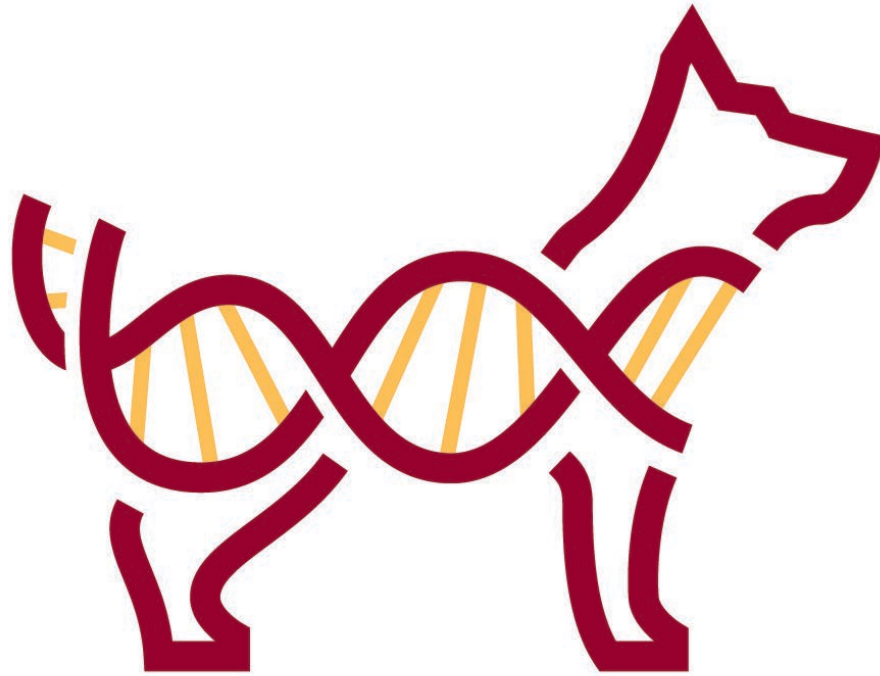


A small genome-wide association study for CaOx in Bichons did not identify a single clear peak

With a complex disease like stones, many dogs are needed to identify and confirm the locations of genetic risk variants



Whole genome sequencing studies are another approach to identify the location of genetic risk factors, particularly for early-onset disease



A whole genome sequencing approach of 6 juvenile bulldogs with CaOx resulted in the discovery of two genetic stone disorders, CaOx1 and CaOx2

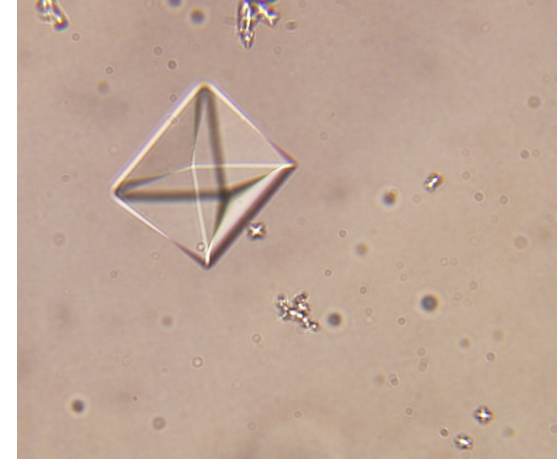
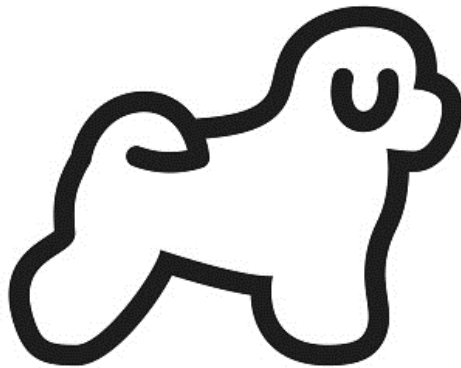


z.umn.edu/caninegenetics

Discovery 5

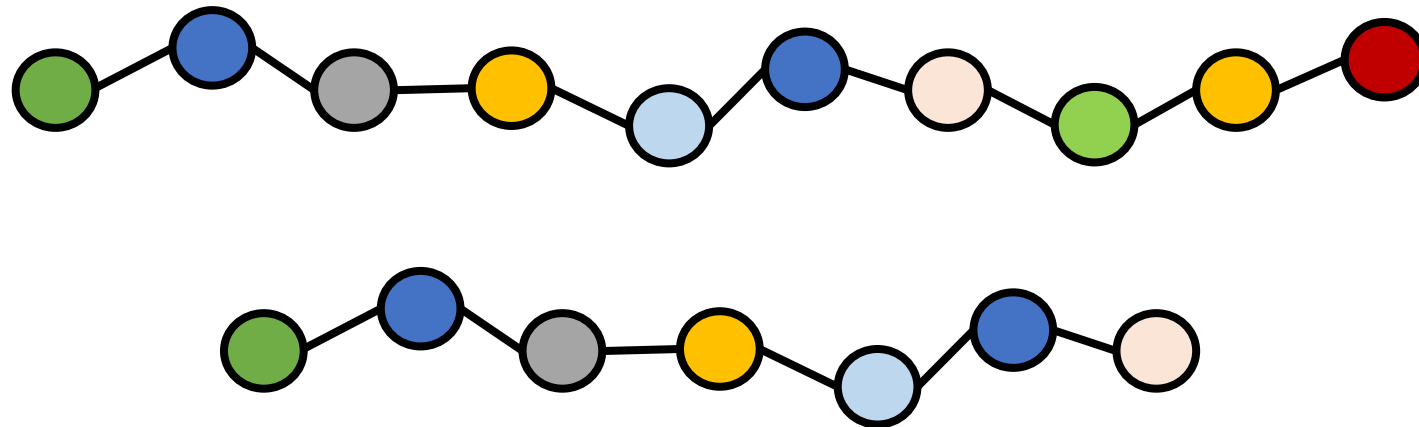
The CaOx1 mutation affects an inhibitor of crystallization

While the mutation itself is not in Bichons, we discovered that the inhibitor affected might also be processed incorrectly in some stone forming Bichons

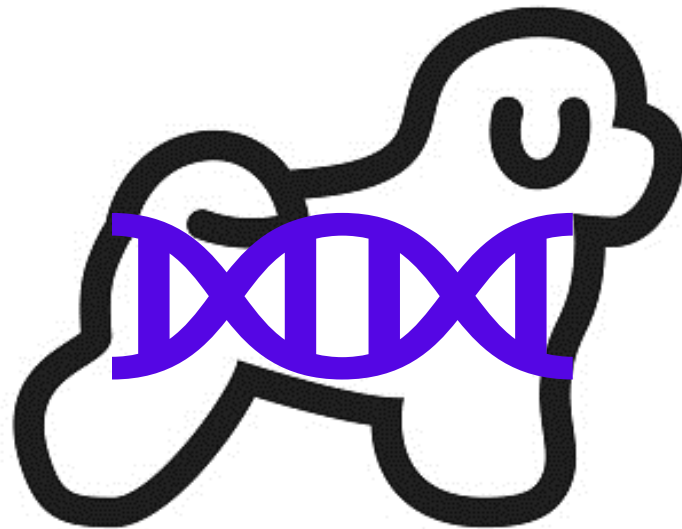


Discovery 5 - Impact

We are continuing to investigate this inhibitor, including whether there are dietary factors or medications that can normalize its processing, thereby reducing CaOx risk



Can we use the whole genome sequencing approach for Bichons?



YES, but this approach works best for early-onset diseases

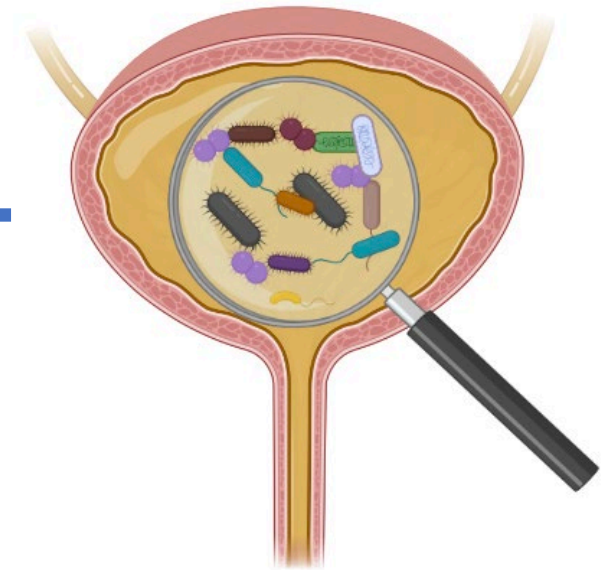
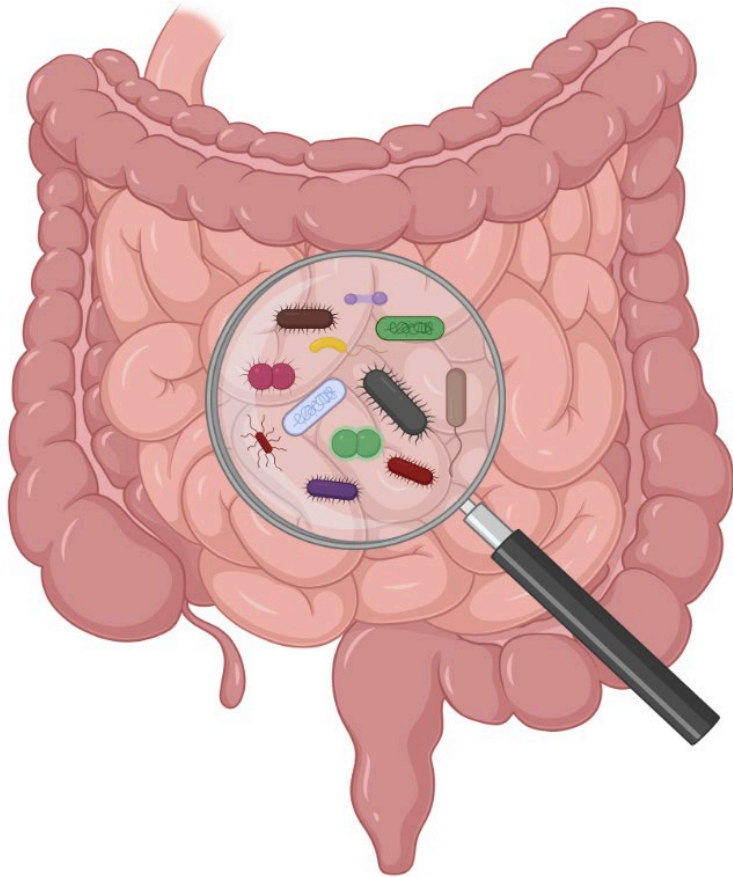
Bichons, while high risk for CaOx in general, rarely form them young



We are currently recruiting more early-onset, recurrent cases in order to have the optimal dogs for a whole genome sequencing study



**Another active area of research is how the microbiome affects
CaOx risk in dogs**



Dr. Emily Coffey

Conclusions

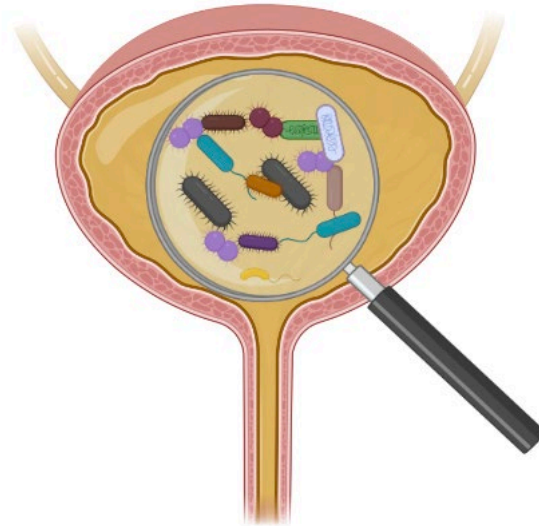
1) Hypercalciuria is a major drivers of CaOx stones in Bichons

[Ca²⁺]



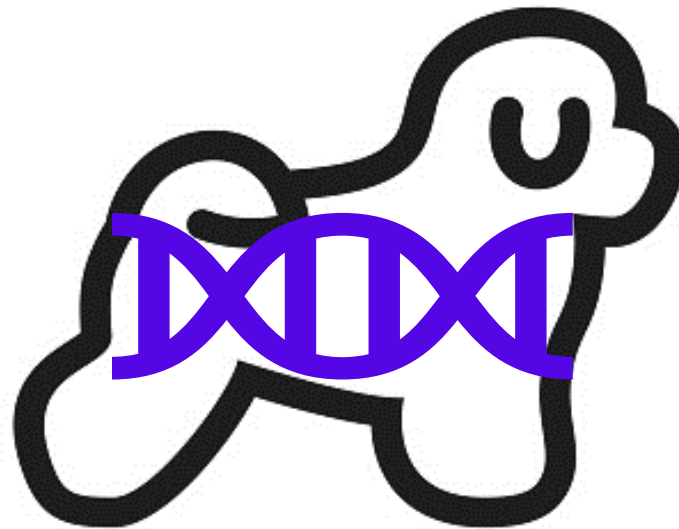
Conclusions

2) Other drivers might include abnormalities in crystallization inhibitors and changes to the microbiome



Conclusions

3) Genetic background is also a risk factor that likely interacts with diet and environment to determine if an individual dog forms stones



Conclusions

3) These discoveries allow us to individualize treatment recommendations for dogs with CaOx stones and generate new ideas for how to prevent and manage them





Acknowledgements



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- Dog study participants and their owners





Questions?

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