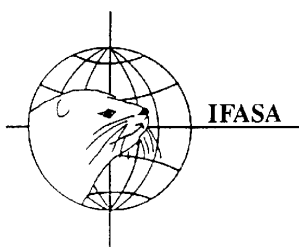
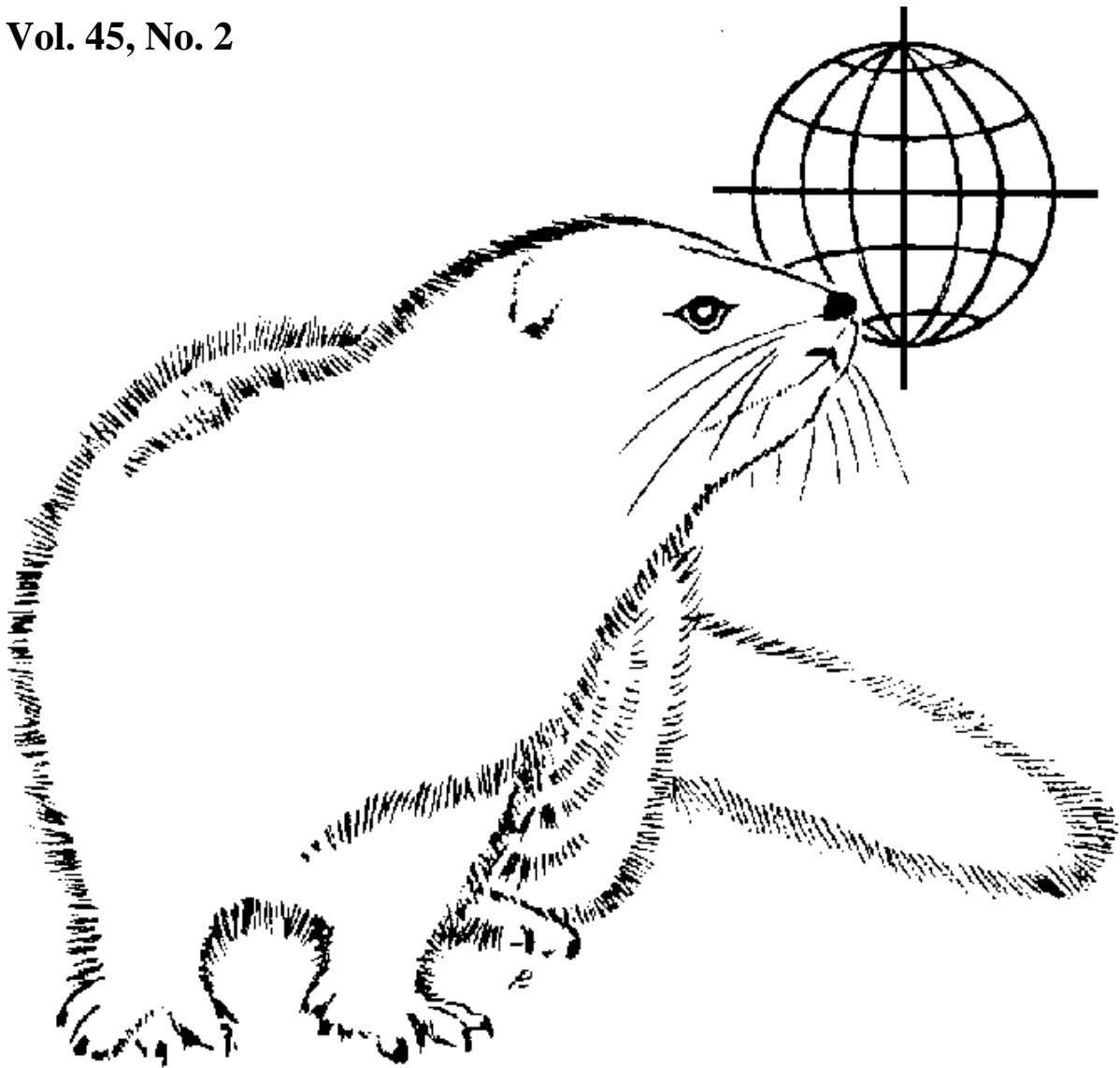


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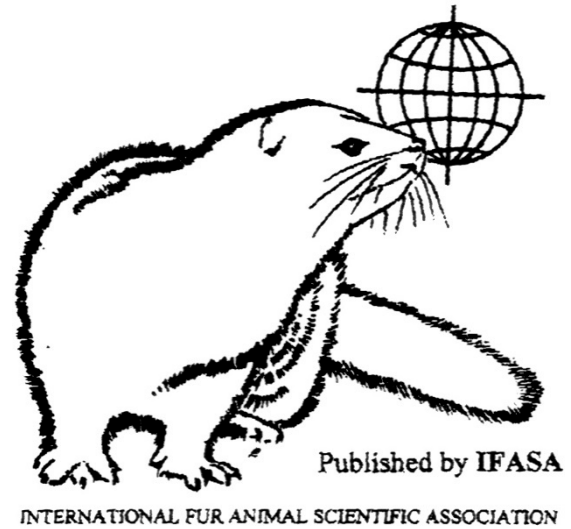
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Notes from the Editor

The SARS CoV-2 is assumed to originate from bats with a presumed but still unknown intermediate host. Further transmission of SARS CoV-2 is from humans to other humans but crossing of species barriers is also seen with transmission from humans to e.g. pets such as cats and dogs and zoo-animals such as tigers, lions and pumas as well as farmed mink.

Focus on farmed mink has been particularly prevalent as the virus spreads rapidly on infected farms. The concern is that the large number of mink constitute a reservoir with potential for creation of mutations that may reduce or eliminate the effect of human vaccines.

SARS CoV-2 has been reported on mink farms in Canada, Denmark, Greece, Italy, Lithuania, the Netherlands, Russia, Spain, Sweden and the United States. In the Netherlands, the Dutch government had already agreed to ban the production in 2024. However, the pandemic led to an earlier phasing out with a final closure of the production by March 2021. In Denmark, the government ordered a culling of all mink including breeding animals in early November 2020, resulting in culling of about 15 million mink. At the same time, a temporary ban of mink production was imposed in Denmark until the end of 2021.

Other countries approach it differently. Russia has developed and registered the world's first COVID-19 vaccine for animals called Carnivac-Cov. The vaccine is developed for dogs, cats, arctic foxes, minks, foxes as well as other animals. The vaccine is highly effective showing 100% efficacy and causes no harm to the animals. Mass production of the vaccine is expected to start in April 2021.

Similarly, in Finland work is at present ongoing, to develop a corona vaccine for mink and Finnraccoon.

It is realised, that urgent action is required to provide an effective vaccine to prevent SARS-CoV-2 infection in Finnish fur farms. So far, no Covid-19 infections have been detected on Finnish fur farms. Overall, the vaccines and rising prices of fur may ensure the production in Finland as well as in other fur producing countries.

While SARS CoV-2 is a new disease challenging fur animal production, Aleutian disease has been a well known threat for a long time. This issue of *Scientifur*, reports from a study, where genomic regions subjected to selection for response to infection with Aleutian mink disease virus were detected in American mink. In another study, developed aptamers were shown to have inhibitory effect on Aleutian mink disease virus production in vitro.

The XII International Scientific Congress in Fur Animal Production (the IFASA Congress) was originally planned to be held in Warsaw, Poland on 25-27 August 2020. Due to the COVID-19 pandemic, the Congress was postponed to 24-26 August 2021. The COVID-19 situation is still uncertain and regulations in countries and on universities differ. For everyone's safety and for a good and cohesive Congress, it is decided that the IFASA Congress 2021 will be held exclusively online. For a follow-up on SARS-CoV-2 issues, a SARS-CoV-2 session is planned at the Congress. The deadline for updating of already submitted abstracts or submissions of new abstracts is 10 May. The deadline for submission of full papers is 31 May. Please, consult the conference webpage (<https://ifasa2020.pl/>) for further information and registration.

Vivi Hunnicke Nielsen

Editor *Scientifur*

BREEDING, GENETICS AND REPRODUCTION**Genetic and phenotypic parameters for body weights, harvest length, and growth curve parameters in American mink**

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Understanding the genetics underlying growth curve is important for selection of animals with better growth potential, but little is known about the genetics of growth curve parameters in mink. This study estimated the genetic parameters for body weights (BW), harvest length (HL), and growth parameters derived from the Richards model. For this purpose, individual BW of 1,088 mink measured seven times in 3-wk intervals (weeks 13 to 31 of life) were used for growth curve modeling using the Richards model. The BW traits included BW at week 13 (BW13), 16 (BW16), 19 (BW19), 22 (BW22), 25 (BW25), 28 (BW28), and 31 (BW31). Univariate analyses indicated that sex and birth-year had significant effects ($P < 0.05$) on BW, HL, asymptotic weight (α), growth rate at mature (k), shape parameter (m), weight at the inflection point (WIP), and age at the inflection point (AIP). In contrast, the color type had only significant effect ($P < 0.05$) on BW31 and HL. Estimated heritabilities (\pm SE) were ranged from 0.36 ± 0.13 (BW13) to 0.46 ± 0.10 (BW22) for BW and were 0.51 ± 0.09 , 0.29 ± 0.09 , 0.30 ± 0.09 , 0.33 ± 0.1 , 0.44 ± 0.10 , and 0.47 ± 0.10 for HL, α , k , m , WIP, and AIP, respectively. The parameter α had non-significant ($P > 0.05$) genetic correlations (\pm SE) with k (-0.21 ± 0.23) and m (-0.10 ± 0.22), suggesting that changing shape parameters (k and m) will not influence asymptotic weight (α). Strong significant ($P < 0.05$) phenotypic (from 0.46 ± 0.03 to 0.60 ± 0.03) and genetic (0.70 ± 0.13 to 0.88 ± 0.09) correlations were observed between HL and different BW measures. The α , AIP, and WIP parameters had significant ($P < 0.05$) genetic correlations with HL indicated that selection for higher α , AIP, and WIP values would increase HL. Parameters k and m had nonsignificant ($P > 0.05$) genetic correlations with HL, indicating the change of the curve shape could not influence HL. Overall, the results suggest that growth curve parameters are heritable and can respond to genetic or genomic selection for optimizing the performance in mink.

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Doi: 10.1093/jas/skab049

How Selective Breeding Has Changed the Morphology of the American Mink (*Neovison vison*) – A Comparative Analysis of Farm and Feral Animals

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Decades of selective breeding carried out on fur farms have changed the morphology, behavior and other features of the American mink, thereby differentiating farm and feral animals. The uniqueness of this situation is not only that we can observe how selective breeding phenotypically and genetically changes successive generations, but also that it enables a comparison of farm minks with their feral counterparts. Such a comparison may thus provide valuable information regarding differences in natural selection and selective breeding. In our study, we found significant morphological differences between farm and feral minks as well as changes in body shape: trapezoidal in feral minks and rectangular in farm minks. Such a clear differentiation between the two populations over a period of several decades highlights the intensity of selective breeding in shaping the morphology of these animals and gives an indication of the speed of phenotypic changes and the species' plasticity. This also suggests that the selective forces (selective breeding vs. natural selection) acting upon body dimensions of minks vary between feral and farm populations.

In this study, we performed a comparative analysis of the morphological traits between feral ($n = 43$) and farm ($n = 200$) individuals of the American mink in Poland to address the question of how multigenerational intensive selective breeding has morphologically differentiated these two populations. Nine body measurements and two proportion coefficients were obtained using adult individuals. The significance of differences between population means was assessed using the Wilcoxon test for independent samples, while the Kruskal–Wallis test was used to compare sex-population groups. Spearman's correlation coefficients between measurements were estimated for each population. We also performed Principal Component Analysis (PCA) to identify the variables that were most closely correlated with variation in the trait measurements and to investigate the morphological differences between farm and feral

minks. We found that the farm minks exhibited significantly higher mean values for eight out of eleven studied traits. Moreover, significant changes in forelimb length, with no concomitant changes in hindlimb length, were accompanied by differences in body shape: trapezoidal in feral minks and rectangular in farm minks. The PCA suggested an almost complete separation of the two populations and indicated that sexes were quite separate; farm males in particular constitute a wholly discrete cluster. Such a clear differentiation between the two populations and sexes over a period of several decades highlights the intensity of selective breeding in shaping the morphology of these animals.

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Doi: 10.3390/ani11010106

Genomic selection in American mink (*Neovison vison*) using a single-step genomic best linear unbiased prediction model for size and quality traits graded on live mink

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Genomic selection relies on single-nucleotide polymorphisms (SNPs), which are often collected using medium-density SNP arrays. In mink, no such array is available; instead, genotyping by sequencing (GBS) can be used to generate marker information. Here, we evaluated the effect of genomic selection for mink using GBS. We compared the estimated breeding values (EBVs) from single-step genomic best linear unbiased prediction (SSGBLUP) models to the EBV from ordinary pedigree-based BLUP models. We analyzed seven size and quality traits from the live grading of brown mink. The phenotype data consisted of ~20,600 records for the seven traits from the mink born between 2013 and 2016. Genotype data included 2,103 mink born between 2010 and 2014, mostly breeding animals. In total, 28,336 SNP markers from 391 scaffolds were available for genomic prediction. The pedigree file included 29,212 mink. The predictive ability was assessed by the correlation (r) between progeny trait deviation (PTD) and EBV, and the regression of PTD on EBV, using 5-fold cross-validation. For each fold, one-fifth of animals born in 2014 formed the validation set. For all

traits, the SSGBLUP model resulted in higher accuracies than the BLUP model. The average increase in accuracy was 15% (between 3% for fur clarity and 28% for body weight). For three traits (body weight, silky appearance of the under wool, and guard hair thickness), the difference in r between the two models was significant ($P < 0.05$). For all traits, the regression slopes of PTD on EBV from SSGBLUP models were closer to 1 than regression slopes from BLUP models, indicating SSGBLUP models resulted in less bias of EBV for selection candidates than the BLUP models. However, the regression coefficients did not differ significantly. In conclusion, the SSGBLUP model is superior to conventional BLUP model in the accurate selection of superior animals, and, thus, it would increase genetic gain in a selective breeding program. In addition, this study shows that GBS data work well in genomic prediction in mink, demonstrating the potential of GBS for genomic selection in livestock species.

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Population Genomics of American Mink Using Whole Genome Sequencing Data

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Characterizing the genetic structure and population history can facilitate the development of genomic breeding strategies for the American mink. In this study, we used the whole genome sequences of 100 mink from the Canadian Centre for Fur Animal Research (CCFAR) at the Dalhousie Faculty of Agriculture (Truro, NS, Canada) and Millbank Fur Farm (Rockwood, ON, Canada) to investigate their population structure, genetic diversity and linkage disequilibrium (LD) patterns. Analysis of molecular variance (AMOVA) indicated that the variation among color-types was significant ($p < 0.001$) and accounted for 18% of the total variation. The admixture analysis revealed that assuming three ancestral populations ($K = 3$) provided the lowest cross-validation error (0.49). The effective population size (N_e) at five generations ago was estimated to be 99 and 50 for CCFAR and Millbank Fur Farm, respectively. The LD patterns revealed that the average r^2 reduced to <0.2 at genomic

distances of >20 kb and >100 kb in CCFAR and Millbank Fur Farm suggesting that the density of 120,000 and 24,000 single nucleotide polymorphisms (SNP) would provide the adequate accuracy of genomic evaluation in these populations, respectively. These results indicated that accounting for admixture is critical for designing the SNP panels for genotype-phenotype association studies of American mink.

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Doi: 10.3390/genes12020258

Detection of selection signatures for response to Aleutian mink disease virus infection in American mink

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Aleutian disease (AD) is the most significant health issue for farmed American mink. The objective of this study was to identify the genomic regions subjected to selection for response to infection with Aleutian mink disease virus (AMDV) in American mink using genotyping by sequencing (GBS) data. A total of 225 black mink were inoculated with AMDV and genotyped using a GBS assay based on the sequencing of *ApeKI*-digested libraries. Five AD-characterized phenotypes were used to assign animals to pairwise groups. Signatures of selection were detected using integrated measurement of fixation index (F_{ST}) and nucleotide diversity ($\theta\pi$), that were validated by haplotype-based (hapFLK) test. The total of 99 putatively selected regions harbouring 63 genes were detected in different groups. The gene ontology revealed numerous genes related to immune response (e.g. *TRAF3IP2*, *WDR7*, *SWAP70*, *CBFB*, and *GPR65*), liver development (e.g. *SULF2*, *SRSF5*) and reproduction process (e.g. *FBXO5*, *CatSperβ*, *CATSPER4*, and *IGF2R*). The hapFLK test supported two strongly selected regions that contained five candidate genes related to immune response, virus–host interaction, reproduction and liver regeneration. This study provided the first map of putative selection signals of response to AMDV infection in American mink, bringing new insights into genomic regions controlling the AD phenotypes.

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High Genetic Diversity of an Invasive Alien Species: Comparison between Fur-Farmed and Feral American Mink (*Neovison vison*) in China

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The American mink (*Neovison vison*) is one of the best-known and most widespread invasive species in China and worldwide. To investigate the genetic characteristics and increase comprehension of the invasiveness process for this species, we compared the genetic characteristics of farmed and feral populations in northeastern China using mitochondrial DNA sequences and microsatellite loci. We found a relatively high diversity among the feral populations that was as high as that of the farmed mink. This demonstrated that high genetic diversity promotes the invasiveness and rapid evolution in the wild.

Genetic characteristics play an important role in alien species for achieving high adaptation and rapid evolution in a new environment. The American mink (*Neovison vison*) is one of the best-known and most widespread invasive species that has successfully invaded the Eurasian mainland over quite a short period, including most parts of northeastern China. However, genetic information on farmed and feral American mink populations introduced in China is completely lacking. In this study, we combined mitochondrial DNA sequences and polymorphic microsatellites to examine the genetic divergence and genetic diversity of farmed and feral American mink populations. Our results suggest that there is admixture of individuals of different genetic characteristics between farmed and feral populations of mink. Furthermore, the genetic diversity of both farmed and feral American mink populations was high, and no bottleneck or population expansion was detected in most of the populations. These findings not only highlight the genetic characteristics of American mink in northeastern China but also contribute to the general understanding of the invasiveness of farmed species.

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Doi: 10.3390/ani11020472

Genome Analysis of Sable Fur Color Links a Lightened Pigmentation Phenotype to a Frameshift Variant in the Tyrosinase-Related Protein 1 Gene

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Sable (*Martes zibellina*) is one of the most valuable species of fur animals. Wild-type sable fur color varies from sandy-yellow to black. Farm breeding and 90 years of directional selection have resulted in a generation of several sable breeds with a completely black coat color. In 2005, an unusually chocolate (pastel) puppy was born in the Puschkinsky State Fur Farm (Russia). We established that the pastel phenotype was inherited as a Mendelian autosomal recessive trait. We performed whole-genome sequencing of the sables with pastel fur color and identified a frameshift variant in the gene encoding membrane-bound tyrosinase-like enzyme (*TYRP1*). *TYRP1* is involved in the stability of the tyrosinase enzyme and participates in the synthesis of eumelanin. These data represent the first reported variant linked to fur color in sables and reveal the molecular genetic basis for pastel color pigmentation. These data are also useful for tracking economically valuable fur traits in sable breeding programs.

Genes (Basel). 2021 Feb; 12 (2): 157.

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Doi: 10.3390/genes12020157

Analysis of *MC1R*, *MITF*, *TYR*, *TYRP1*, and *MLPH* Genes Polymorphism in Four Rabbit Breeds with Different Coat Colors

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Coat color is an important breed characteristic and economic trait for rabbits, and it is regulated by a few genes. In this study, the gene frequencies of some pigmentation genes were investigated in four Chinese native rabbit breeds with different coat colors. A total of 14 genetic variants were detected in the gene fragments of *MC1R*, *MITF*, *TYR*, *TYRP1*, and *MLPH* genes, and there was low-to-moderate polymorphism in the populations. The gene frequency showed significant differences among the four rabbit populations. The above results suggest that these genetic variations play an important role in regulating the coat color of rabbits. This study will provide potential molecular markers for the breeding of coat color traits in rabbits.

Pigmentation genes such as *MC1R*, *MITF*, *TYR*, *TYRP1*, and *MLPH* play a major role in rabbit coat color. To understand the genotypic profile underlying coat color in indigenous Chinese rabbit breeds, portions of the above-mentioned genes were amplified and variations in them were analyzed by DNA sequencing. Based on the analysis of 24 Tianfu black rabbits, 24 Sichuan white rabbits, 24 Sichuan gray rabbits, and 24 Fujian yellow rabbits, two indels in *MC1R*, three SNPs in *MITF*, five SNPs (single nucleotide polymorphisms) in *TYR*, one SNP in *TYRP1*, and three SNPs in *MLPH* were discovered. These variations have low-to-moderate polymorphism, and there are significant differences in their distribution among the different breeds ($p < 0.05$). These results provide more information regarding the genetic background of these native rabbit breeds and reveal their high-quality genetic resources.

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Lipid droplets in mammalian eggs are utilized during embryonic diapause

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Developmental Biology

Declined expressing mRNA of beta-defensin 108 from epididymis is associated with decreased sperm motility in blue fox (*Vulpes lagopus*)

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Background

Fecundity is important for farm blue fox (*Vulpes lagopus*), who with asthenospermia have been a problem in some of farms in China. A key symptom of asthenospermia is decreased sperm motility. The decreased secreting beta-defensin108 (*vBD108*) of blue fox is speculated to be related to asthenospermia. To clarify this idea, the mRNA expression of *vBD108* in testis and epididymis of blue foxes with asthenospermia were detected and compared to the healthy one. The antibody was prepared and analyzed by immunohistochemistry.

Results

The *vBD108* in testis and epididymis was found both in blue fox with asthenospermia and healthy group by the method of immunohistochemistry. The expression of *vBD108* mRNA in testes ($P < 0.05$) and epididymal corpus ($P < 0.0001$) in asthenospermia group was lower than that in healthy group.

Conclusions

These results suggested that *vBD108* deficiency may be related to blue fox asthenospermia. Meanwhile, the study on the blue fox *vBD108* provides a hopeful direction to explore the pathogenesis of blue fox asthenospermia in the future.

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NUTRITION, FEEDING AND MANAGEMENT

Absorption of α -tocopheryl acetate is limited in mink kits (*Mustela vison*) during weaning

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Bioavailability of α -tocopherol varies with source, dose and duration of supplementation. The effect of source and dose of α -tocopherol on response of α -tocopherol stereoisomers in plasma and tissues of mink kits during the weaning period was studied. Twelve mink kits were euthanised in CO₂ at the beginning of the experiment, and 156 mink kits (12 replicates per treatment group) were randomly assigned to thirteen treatment groups: no added α -tocopherol in the feed (0 dose) or four different doses (50, 75, 100 and 150 mg/kg of diet) of RRR- α -tocopherol (ALC), RRR- α -tocopheryl acetate (ACT) or *all-rac*- α -tocopheryl acetate (SYN). Six mink kits per treatment group were euthanised 3 weeks after initiation of the experiment, and the remaining six were euthanised 6 weeks after initiation of the experiment. The RRR- α -tocopherol content in plasma, liver, heart and lungs was affected by interaction between source and dose ($P < 0.01$ for all). The highest RRR- α -tocopherol content in plasma (13.6 μ g/ml; LS-means for source across dose and week), liver (13.6 μ g/mg), heart (7.6 μ g/mg) and lungs (9.8 μ g/mg) was observed

in mink kits fed ALC. The RRR- α -tocopherol content in plasma and tissues depended on source and dose interaction and increased linearly with supplementation. In conclusion, the interaction between source and dose reveals a limitation in hydrolysis of ester bond in α -tocopheryl acetate in mink kits around weaning as the likely causative explanation for the higher response of ALC at the highest doses. Thus, considerable attention has to be paid to the source of α -tocopherol during weaning of mink kits fed a high dose of α -tocopherol.

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Estimation of the Age and Reproductive Performance of Wild-Born and Escaped Mink (*Neovison vison*) Caught in the Wild in Denmark

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Previous studies of wild caught mink in Denmark showed that 30–80% had recently escaped from farms. Therefore, it is debated whether a self-sustaining feral mink population is established in Denmark or whether the population rests upon a continuous contribution of captive-born farm mink. Knowledge regarding the reproduction and mortality of mink adapted for living in the wild is important for the management of feral mink. In this study, we separated wild-born from captive-born mink caught in the wild in Denmark. To be able to age the mink in this study, an age determination model for mink was developed based on the width of the pulp cavity. The mean litter size of wild-born female mink was 7.6 (range: 5–11 kits). The annual turnover of mink caught in the wild was estimated to be 66%, and the yearly mortality was 69%; thus, the population of wild-born mink is slightly declining. The results confirmed that the wild-born mink population in Denmark is re-

producing and self-sustaining without a continuous influx of captive-born mink escaped from farms. The effect of escaped mink on the wild mink population will depend on the currently unknown ability of captive mink to survive in the wild.

The feral mink population in Denmark consists of two groups of animals: mink born in the wild and mink that have recently escaped from farms. The aims of this study were to: (1) estimate the reproductive performance and mortality of the Danish mink born in the wild (wild-born) and mink escaped from farms (captive-born); (2) discuss the likelihood of a self-sustaining population of wild-born mink in Denmark; and (3) model the relationship between the pulp cavity width and the age of mink. During 2018, 247 wild caught mink were sent for necropsy at the Danish National Veterinary Institute. Based on body length, 112 were determined as captive-born and 96 as wild-born. The mean litter size \pm SE of wild-born females was 7.6 ± 0.9 (range: 5–11 kits) and for captive-born females 5.9 ± 0.9 (range: 1–10 kits). The relationship between age (in months) of mink and pulp cavity width was highly significant. Individuals with a pulp cavity width of $>35\%$ were younger than one year. Based on fecundity, the turnover of the mink population was estimated to be 66%, and the yearly mortality was estimated at 69%. Hence, the population is slightly declining. In conclusion, a feral reproducing mink population in Denmark persists without a continuous influx of captive-born mink from farms.

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Geometric morphometric investigation of craniofacial morphological change in domesticated silver foxes

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To test the effects of domestication on craniofacial skeletal morphology, we used three-dimensional geometric morphometrics (GM) along with linear and endocranial measurements to compare selected (domesticated) and unselected foxes from the Russian Farm-Fox Experiment to wild foxes from the progenitor population from which the farmed foxes are derived. Contrary to previous findings, we find that domesticated

and unselected foxes show minimal differences in craniofacial shape and size compared to the more substantial differences between the wild foxes and both populations of farmed foxes. GM analyses and linear measurements demonstrate that wild foxes differ from farmed foxes largely in terms of less cranial base flexion, relatively expanded cranial vaults, and increased endocranial volumes. These results challenge the assumption that the unselected population of foxes kept as part of the Russian Farm-Fox experiment are an appropriate proxy for 'wild' foxes in terms of craniofacial morphology and highlight the need to include wild populations in further studies of domestication syndrome to disentangle the phenotypic effects of multiple selection pressures. These findings also suggest that marked increases in docility cannot be reliably diagnosed from shape differences in craniofacial skeletal morphology.

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BEHAVIOUR AND WELFARE

One welfare impacts of COVID-19 – A summary of key highlights within the one welfare framework

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HEALTH AND DISEASE

Aptamer-targeting of Aleutian mink disease virus (AMDV) can be an effective strategy to inhibit virus replication

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Aleutian mink disease (AMD), which is caused by Aleutian mink disease virus (AMDV), is an important contagious disease for which no effective vaccine is yet available. AMD causes major economic losses for mink farmers globally and threatens some carnivores such as skunks, genets, foxes and raccoons. Aptamers have exciting potential for the diagnosis and/or treatment of infectious viral diseases, including AMD. Using a magnetic beads-based systemic evolution of ligands by exponential enrichment (SELEX) approach, we have developed aptamers with activity against AMDV after 10 rounds of selection. After incubation with the ADVa012 aptamer (4 µM) for 48 h, the concentration of AMDV in the supernatant of infected cells was 47% lower than in the supernatant of untreated cells, whereas a random library of aptamers has no effect. The half-life of ADVa012 was ~32 h, which is significantly longer than that of other aptamers. Sequences and three dimensions structural modeling of selected aptamers indicated that they fold into similar stem-loop structures, which may be a preferred structure for binding to the target protein. The ADVa012 aptamer was shown to have an effective and long-lasting inhibitory effect on viral production in vitro.

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Monitoring of SARS-CoV-2 infection in mustelids

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American mink and ferret are highly susceptible to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), but no information is available for other mustelid species. SARS-CoV-2 spreads very efficiently within mink farms once introduced, by direct and indirect contact, high within-farm animal density increases the chance for transmission. Between-farm spread is likely to occur once SARS-CoV-2 is introduced, short distance between SARS-CoV-2 positive farms is a risk factor. As of 29 January 2021, SARS-CoV-2 virus has been reported in 400 mink farms in eight countries in

the European Union. In most cases, the likely introduction of SARS-CoV-2 infection into farms was infected humans. Human health can be at risk by mink-related variant viruses, which can establish circulation in the community, but so far these have not shown to be more transmissible or causing more severe impact compared with other circulating SARS-CoV-2. Concerning animal health risk posed by SARS-CoV-2 infection the animal species that may be included in monitoring plans are American mink, ferrets, cats, raccoon dogs, white-tailed deer and Rhinolophidae bats. All mink farms should be considered at risk of infection; therefore, the monitoring objective should be early detection. This includes passive monitoring (in place in the whole territory of all countries where animals susceptible to SARS-CoV-2 are bred) but also active monitoring by regular testing. First, frequent testing of farm personnel and all people in contact with the animals is recommended. Furthermore randomly selected animals (dead or sick animals should be included) should be tested using reverse transcriptase-polymerase chain reaction (RT-PCR), ideally at weekly intervals (i.e. design prevalence approximately 5% in each epidemiological unit, to be assessed case by case). Suspected animals (dead or with clinical signs and a minimum five animals) should be tested for confirmation of SARS-CoV-2 infection. Positive samples from each farm should be sequenced to monitor virus evolution and results publicly shared.

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Coronaviruses Associated with the Superfamily *Musteloidea*

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Among the animal superfamily *Musteloidea*, which includes those commonly known as mustelids, naturally occurring and species-specific alphacoronavirus infections have been observed in both mink (*Mustela vison/Neovison vison*) and domestic ferrets (*Mustela*

putorius furo). Ferret systemic coronavirus (FRSCV), in particular, has been associated with a rare but fatal systemic disease. In recent months, it has become apparent that both minks and ferrets are susceptible to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), a betacoronavirus and the cause of the coronavirus disease 2019 (COVID-19) pandemic. Several mink farms have experienced SARS-CoV-2 outbreaks, and experimental models have demonstrated susceptibility of ferrets to SARS-CoV-2. The potential for pet ferrets to become infected with SARS-CoV-2, however, remains elusive. During the 2002–2003 SARS epidemic, it was also apparent that ferrets were susceptible to SARS-CoV and could be utilized in vaccine development. From a comparative standpoint, understanding the relationships between different infections and disease pathogenesis in the animal superfamily *Musteloidea* may help elucidate viral infection and transmission mechanisms, as well as treatment and prevention strategies for coronaviruses.

mBio. 2021 Jan-Feb; 12 (1): e02873-20.
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Doi: 10.1128/mBio.02873-20

Preliminary report of an outbreak of SARS-CoV-2 in mink and mink farmers associated with community spread, Denmark, June to November 2020

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In June–November 2020, SARS-CoV-2-infected mink were detected in 290 of 1,147 Danish mink farms. In North Denmark Region, 30% (324/1,092) of people found connected to mink farms tested SARS-CoV-2-PCR-positive and approximately 27% (95% confidence interval (CI): 25–30) of SARS-CoV-2-strains from humans in the community were mink-associated. Measures proved insufficient to mitigate spread. On 4 November, the government ordered culling of all Danish mink. Farmed mink constitute a potential virus reservoir challenging pandemic control.

Euro Surveill. 2021 Feb 4; 26 (5): 2100009.
Doi: 10.2807/1560-7917.ES.2021.26.5.210009

SARS-CoV-2 in Danish Mink Farms: Course of the Epidemic and a Descriptive Analysis of the Outbreaks in 2020

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Since 2019, SARS-CoV-2 has spread and become a global pandemic. Unexpectedly, infection of farmed mink by SARS-CoV-2 was detected in the Netherlands in April 2020 and infections in three mink farms in Denmark were detected in June. Approximately 1140 mink farms were present in Denmark at the time, and a rapid increase in the number of farms with infected mink occurred from September onwards. Features of the infection on these farms were examined and potential routes of transmission between farms evaluated. It is apparent that the infection spread very easily between mink within a farm and can spread to and from people with close contact to the farmed mink. The infection spread between farms in close proximity to each other, but direct human contact is still the only identified route of virus transmission.

SARS-CoV-2 infection is the cause of COVID-19 in humans. In April 2020, SARS-CoV-2 infection in farmed mink (*Neovision vision*) occurred in the Netherlands. The first outbreaks in Denmark were detected in June 2020 in three farms. A steep increase in the number of infected farms occurred from September and onwards. Here, we describe prevalence data collected from 215 infected mink farms to characterize spread and impact of disease in infected farms. In one third of

the farms, no clinical signs were observed. In farms with clinical signs, decreased feed intake, increased mortality and respiratory symptoms were most frequently observed, during a limited time period (median of 11 days). In 65% and 69% of farms, virus and seroconversion, respectively, were detected in 100% of sampled animals at the first sampling. SARS-CoV-2 was detected, at low levels, in air samples collected close to the mink, on mink fur, on flies, on the foot of a seagull, and in gutter water, but not in feed. Some dogs and cats from infected farms tested positive for the virus. Chickens, rabbits, and horses sampled on a few farms, and wildlife sampled in the vicinity of the infected farms did not test positive for SARS-CoV-2. Thus, mink are highly susceptible to infection by SARS-CoV-2, but routes of transmission between farms, other than by direct human contact, are unclear.

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Corona's new coat: SARS-CoV-2 in Danish minks and implications for travel medicine

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Doi: 10.1016/j.tmaid.2020.101922

SARS-CoV-2 Exposure in Escaped Mink, Utah, USA

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In August 2020, outbreaks of coronavirus disease were confirmed on mink farms in Utah, USA. We surveyed mammals captured on and around farms for evidence of infection or exposure. Free-ranging mink, presumed domestic escapees, exhibited high antibody titers, suggesting a potential severe acute respiratory syndrome coronavirus 2 transmission pathway to native wildlife.

Emerg Infect Dis. 2021 Mar; 27 (3): 988–990.
Doi: 10.3201/eid2703.204444

Replication, pathogenicity, and transmission of SARS-CoV-2 in minks

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Minks are raised in many countries and have transmitted severe acute respiratory syndrome–coronavirus 2 (SARS-CoV-2) to humans. However, the biologic properties of SARS-CoV-2 in minks are largely unknown. Here, we investigated and found that SARS-CoV-2 replicates efficiently in both the upper and lower respiratory tracts, and transmits efficiently in minks via respiratory droplets; pulmonary lesions caused by SARS-CoV-2 in minks are similar to those seen in humans with COVID-19. We further found that a spike protein-based subunit vaccine largely prevented SARS-CoV-2 replication and lung damage caused by SARS-CoV-2 infection in minks. Our study indicates that minks are a useful animal model for evaluating the efficacy of drugs or vaccines against COVID-19 and that vaccination is a potential strategy to prevent minks from transmitting SARS-CoV-2.

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Possible host-adaptation of SARS-CoV-2 due to improved ACE2 receptor binding in mink

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Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections on mink farms are increasingly observed in several countries, leading to the massive culling of animals on affected farms. Recent studies showed multiple (anthropo)zoonotic transmission events between humans and mink on these farms. Mink-derived SARS-CoV-2 sequences from The Netherlands and Denmark contain multiple substitutions in the S protein receptor binding domain (RBD). Molecular modeling showed that these substitutions increase the mean binding energy, suggestive of potential adaptation of the SARS-CoV-2 S protein to the mink angiotensin-converting enzyme 2 (ACE2) receptor. These substitutions could possibly also impact human ACE2 binding affinity as well as humoral immune responses directed to the RBD region of the SARS-CoV-2 S protein in humans. We wish to highlight these observations to raise awareness and urge for the continued surveillance of mink (and other animal)-related infections.

Virus Evol. 2021 Jan 4;7 (1): veaa094.
eCollection 2021 Jan.
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Doi: 10.1093/ve/veaa094

The SARS-CoV-2 Y453F mink variant displays a pronounced increase in ACE-2 affinity but does not challenge antibody neutralization

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SARS-CoV-2 infection in farmed minks, associated zoonotic concerns, and importance of the One Health approach during the ongoing COVID-19 pandemic

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The coronavirus disease 2019 (COVID-19) pandemic has now affected over 72.5 million people worldwide, with nearly 1.6 million deaths reported globally as of December 17, 2020. SARS-CoV-2 has been implicated to have originated from bats and pangolins, and its intermediate animal hosts are being investigated. Crossing of the species barrier and exhibition of zoonosis have been reported in SARS-CoV-2 in farm (minks), domesticated (cats and dogs), and wild animals (tigers, puma, and lions). Recently, the rapid spread of SARS-CoV-2 infection was reported in mink farms, which led to the death of a myriad minks. The clinical and pathological findings of SARS-CoV-2 infection and the rapid animal-to-animal transmission in minks are almost similar to the findings observed in patients with COVID-19. Additionally, the rapid virus transmission among minks and the associated mutations resulted in a new mink-associated variant that was identified in both minks and humans, thereby providing evidence of mink-to-human transmission of SARS-CoV-2. The new mink-associated SARS-CoV-2 variant with a possible reduced sensitivity to neutralizing antibodies poses serious risks and is expected to have a direct effect on the diagnostic techniques, therapeutics, and vaccines that are currently under development. This article highlights the current evidence of SARS-CoV-2

infection in farmed minks, and provides an understanding of the pathogenesis of COVID-19 in minks and the associated zoonotic concerns of SARS-CoV-2 transmission from minks to humans with an emphasis on appropriate mitigation measures and on the necessity of adopting the One Health approach during the COVID-19 pandemic.

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SARS-CoV-2 variants lacking ORF8 occurred in farmed mink and pangolin

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COVID-19 in Farm Animals: Host Susceptibility and Prevention Strategies

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The outbreak of SARS-CoV-2 (also known as COVID-19) has caused pandemic diseases among humans globally so far. The COVID-19 infections were also reported on farm and pet animals, which were discussed and summarized in this study. Although the damage of COVID-19 has not been reported as serious as highly pathogenic avian influenza (HPAI) for poultry and African Swine Fever (ASF) for pigs on commercial farms so far, the transmission mechanism of COVID-19 among group animals/farms and its long-term impacts are still not clear. Prior to the development of the effec-

tive vaccine, the biosecurity measures (e.g., conventional disinfection strategies and innovated technologies) may play roles in preventing potential spread of diseases/viruses.

COVID-19 is caused by the virus SARS-CoV-2 that belongs to the family of Coronaviridae, which has affected multiple species and demonstrated zoonotic potential. The COVID-19 infections have been reported on farm animals (e.g., minks) and pets, which were discussed and summarized in this study. Although the damage of COVID-19 has not been reported as serious as highly pathogenic avian influenza (HPAI) for poultry and African Swine Fever (ASF) for pigs on commercial farms so far, the transmission mechanism of COVID-19 among group animals/farms and its long-term impacts are still not clear. Prior to the marketing of efficient vaccines for livestock and animals, on-farm biosecurity measures (e.g., conventional disinfection strategies and innovated technologies) need to be considered or innovated in preventing the direct contact spread or the airborne transmission of COVID-19.

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Third update on possible animal sources for human COVID-19

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SARS-CoV-2 emerged in the human population towards the end of 2019 and has been spreading at an alarming rate and cases in humans continue to increase. This is predicted to continue until commercial vaccines, which recently became available in selected countries (<https://www.bbc.co.uk/news/uk-55227325>), are approved and have been distributed to a larger number of people, ensuring that a certain proportion of the global population is protected. Pet animals such as cats and dogs do not currently appear to pose a risk to humans; however, continuous monitoring of these animals is warranted. SARS-CoV-2 spillover into farm animals has not been reported to date, but if it happens, it likely happens very sporadically and involves a low

number of animals. An exception to this is farmed mink, where SARS-CoV-2 spreads quickly and causes clinical disease in infected animals. As a precaution, nearly all affected mink farms implemented immediate mass culling. The rapid identification of a human-animal spillover event and its removal or containment is critical in safeguarding humans and also other animal species. Careful consideration and attention should be given to other future SARS-CoV-2 spillover events into the animal population in order to effectively control the ongoing pandemic.

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Bats, pangolins, minks and other animals - villains or victims of SARS-CoV-2?

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Mink SLAM V-Region V74I Substitutions Contribute to the Formation of Syncytia Induced by Canine Distemper Virus

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The Signal lymphatic activation molecule (SLAM, also known as CD150) as the cellular receptor of canine distemper virus (CDV) plays an important role in the virus-host interaction. However, it is still unknown whether amino acid differences in the SLAM variable (V) region affect the formation of syncytia. Here, using raccoon dog SLAM (rSLAM) and mink SLAM (mSLAM), we performed SLAM-V homologous modeling, site-directed mutagenesis, and surface expression analysis, as well as a cell fusion assay, to study the interaction between SLAM and CDV. More specifically, our investigation focused on two amino acid residues (74 and 129) of SLAM, previously predicted to play a relevant role in receptor-ligand interaction. Our results indicated that only residues at position 60, 74, and 129 were different between rSLAM and mSLAM among the 29 amino acids that might interact with CDV H, and residues 74 and 129 were located in the interface region interacting with CDV H. The amino acid substitution at the positions of 74 have a significant effect on the expression of mSLAM. The SLAM-V74I mutation in mink significantly improved the cell fusion efficiency of CDV. In contrast, the SLAM-I74V mutation in the raccoon dog significantly decreased cell fusion efficiency. We conclude that residue 74 of SLAM plays an important role during the the formation of syncytia. Only when implementing CDV infection analysis, the rSLAM-Q129R can significantly decreased the mean number of syncytia, but the mSLAM-R129Q can't. Additionally, residue 60 show variability between rSLAM and mSLAM. We believe that our study makes a significant contribution to the literature because we provide molecular data, partially accounting for the differences in host membrane and virus interaction laying the foundation for further molecular work.

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Genome Sequence of a Minacovirus Strain from a Farmed Mink in The Netherlands

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ABSTRACT We report the genome sequence of a Minacovirus strain identified from a fecal sample from a farmed mink (*Neovison vison*) in The Netherlands that was tested negative for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) using real-time PCR (RT-PCR). The viral genome sequence was obtained using agnostic deep sequencing.

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Digestive tract nematode infections in non-native invasive American mink with the first molecular identification of *Molineus patens*

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Evaluating a tylosin dosage regimen for treatment of *Staphylococcus delphini* infection in mink (*Neovison vison*): a pharmacokinetic-pharmacodynamic approach

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Abstract *Staphylococcus delphini* is one of the most common pathogens isolated from mink infections, especially dermatitis. Tylosin (TYL) is used frequently against these infections, although no evidence-based treatment regimen exists. This study aimed to explore the dosage of TYL for infections caused by *S. delphini* in mink. Two animal experiments with a total of 12 minks were conducted to study the serum pharmacokinetic (PK) characteristics of TYL in mink after 10 mg/kg IV and oral dosing, respectively. The concentration of TYL in serum samples collected before and eight times during 24 h after TYL administration was quantitated with liquid chromatography quadrupole time-of-flight mass spectrometry, and the TYL disposition was analyzed using non-linear mixed effect analysis. The pharmacodynamics (PD) of TYL against *S. delphini* were studied using semi-mechanistic modeling of in vitro time-kill experiments. PKPD modeling and simulation were done to establish the PKPD index and dosage regimen. The disposition of TYL was described by a two-compartmental model. The area under the free concentration–time curve of TYL over the minimum inhibitory concentration of *S. delphini* (fAUC/MIC) was determined as PKPD index with breakpoints of 48.9 and 98.7 h for bacteriostatic and bactericidal effect, respectively. The calculated daily oral dose of TYL was 2378 mg/kg, which is 238-fold higher than the currently used TYL oral dosage regimen in mink (10 mg/kg). Accordingly, sufficient TYL concentrations are impossible to achieve in mink plasma, and use of this drug for extra-intestinal infections in this animal species must be discouraged.

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Nielsen, V.H., Møller, S.H., Hansen, B.K. & Berg, P. (2007). Genotype - environment interaction in mink. *Scientifur*, 31 (3), 89.

Shirali, M., Nielsen, V.H., Møller S.H. & Jensen, J. (2015). Longitudinal analysis of residual feed intake and BW in mink using random regression with heterogeneous residual variance. *Animal*, 8 (10), 1597-1604.