Proceedings, 10th World Congress of Genetics Applied to Livestock Production

Single nucleotide polymorphisms in the DRD2 and XKR4 genes may be beneficial to Missouri beef cattle grazing endophyte-infected tall fescue

***K.M. Ely*[1], A. M. Saxton[1], T. R. Lock[2], R. L. Kallenbach[2], C.J. Kojima[1]**
[1]University of Tennessee, [2]University of Missouri

Abstract: Decreased growth, fertility and lactation can be observed in beef cattle grazing endophyte-infected tall fescue. Polymorphisms in the DRD2 and XKR4 genes may modulate these responses. Adjusted birth (ABW) and 205 day weights (A205) were calculated for 1,697 calves from 390 dams, over a span of 14 years, at the Forage Systems Research Center located near Linneus, Missouri. These represented two herds (fall- and spring-calving) of Angus-crossed beef cattle grazing endophyte-infected tall fescue. Fall-born calves had lighter ABW and A205 than spring-born calves ($p<0.0001$). Dam genotype at DRD2 and XKR4 influenced A205 ($p=0.0015$ and $p=0.0152$ respectively). There was an interaction noted between DRD2 and season; spring calves from AA and AG dams had higher A205 ($p=0.021$). No genotype effect on ABW was observed. Dam genotype at these loci may affect calf growth when stock are consuming endophyte-infected tall fescue, possibly through modulation of lactation.
Keywords: DRD2; XKR4; fescue toxicosis

Introduction

Tall fescue (*Lolium arundinaceum Schreb.*), a cool-season perennial bunch grass, is the most widely used forage in the southeastern United States (Stuedemann and Hoveland (1988)). Tall fescue is popular with forage/livestock producers due to its quick establishment and ability to withstand drought and over-grazing. The resilience of tall fescue is partly due to a symbiotic relationship with an endophytic fungus (*N. coenophialum*). The endophyte produces ergot alkaloids - primarily the dopamine agonist ergovaline - which when ingested by cattle has many negative side effects. Some of these side effects include decreased reproductive efficiency, vasoconstriction, reduction in dry matter intake, and in extreme cases, necrosis of the extremities (Fribourg et al. (1991)). Lactation has also been shown to be compromised, thought to be either due to reduced feed intake or decreased serum prolactin (Porter and Thompson (1992)). This collection of symptoms is often referred to as fescue toxicosis and costs the beef industry more than $150 million annually.

Previous research on beef cattle in Tennessee has shown that a single nucleotide polymorphism (SNP) in the dopamine receptor D2 (DRD2) gene regulates prolactin secretion (rs41749780; Campbell et al. (2014)). Decreased serum prolactin concentration is commonly noted as an indicator of fescue toxicosis (Schillo et al. (1988)). Domperidone, a dopamine antagonist, has been shown in horses to reduce the effects of fescue toxicosis in pregnant mares grazing endophyte-infected tall fescue (Cross et al. (2012)). Dopamine D2 antagonism increases prolactin secretion (Ben-Jonathan and Hnasko (2000)). This SNP in the DRD2 gene has shown to increase prolactin concentrations with the possibility that the 'A' allele in spring calving herds is mitigating the effects of fescue toxicosis (Campbell et al. (2014)).

The XK, kell blood group complex, subunit-related family, member 4 (XKR4) gene is sparsely mentioned in the literature. Previous research in humans has evaluated XKR4 genotype with efficacy of schizophrenia treatment using iloperidone, a dopamine antagonist related to domperidone (Lavedan et al. (2009); Fijal et al. (2012)); treatment with iloperidone is associated with an elevation in prolactin (Jain (2000); Cutler et al. (2008)). A study in cattle has shown 3 SNP in the XKR4 gene to be associated with subcutaneous rump fat (rs42646645, rs42646708 and rs41724387; Porto Neto et al. (2012)). Bastin et al. (in press) found an association with a SNP (rs42646708) in the XKR4 gene and increased prolactin concentrations.

The purpose of this study was to examine the possible effects of DRD2 and XKR4 genotypes on adjusted 205-day weaning weight (A205) and adjusted birth weight (ABW) on a large herd of beef cattle grazing endophyte-infected tall fescue in Missouri.

Materials and Methods

Data. Data were recorded on 1,697 calves from 390 dams at the Forage Systems Research Center (FSRC) located near Linneus, Missouri. Calf data was collected over a span of 14 years. This is an Angus-crossed beef cattle herd that is well maintained and has an active cull rate. Custom Taqman assays (Applied Biosystems, Carlsbad, CA) for the DRD2 and XKR4 SNP (rs41749780 and rs42646645 respectively) were used to genotype the herd at FSRC; phenotypes assessed were birth weight and weaning weight. These were adjusted for age of dam, sex of calf, and age at weaning (Beef Improvement Federation (2010)) to provide A205 and ABW phenotypes. This herd grazed pasture that is primarily endophyte-infected tall fescue.

Statistical analysis. Dam genotype and allele frequencies for DRD2 and XKR4 are listed in table 1. The dam XKR4 GG genotype was sparsely represented in the popula-

tion, f(GG) = 0.01, therefore it was dropped from the analysis. The model for each phenotype included the fixed effects of dam genotype, season, and their interaction. Year was included as a random effect. The analysis was run using mixed model analysis of variance in SAS 9.3 (Cary, N.C.) as a randomized block design. Least squares means (+/- SEM) were compared using Fisher's protected least significant difference.

Table 1: Dam genotypic and allelic frequencies of DRD2 and XKR4

Dam Genotype	f(AA)	f(AG)	f(GG)	f(A)	f(G)
DRD2	0.26	0.47	0.27	0.49	0.51
XKR4	0.85	0.14	0.01	0.92	0.08

Results and Discussion

Adjusted birth weight. Neither dam DRD2 nor XKR4 genotype affected ABW (p=0.46 and p=0.49 respectively). An effect of season on ABW was observed (p<0.0001); fall- born calves exhibited lower ABW (33.8 +/- 0.4 kg) than spring-born calves (37.3 +/- 0.3 kg).

Adjusted 205-day weaning weight. An effect of season on A205 (p<0.0001) was observed such that fall-born calves exhibited lower A205 (see table 2) than spring-born calves. Dam genotype for DRD2 influenced A205 (p=0.0015) such that calves from AA and AG dams had higher A205 than those from GG dams. There was an interaction between season and dam DRD2 genotype (p=0.021) due to smaller seasonal differences in AA dams as compared to genotypes with the G allele.

Table 2: Effect of Dam DRD2 genotype on A205[1]

Season\DRD2	AA	AG	GG	Average
Fall	$224^{C,2}$	220^{C}	213^{D}	219
Spring	243^{AB}	247^{A}	243^{B}	244
Average	234	233	228	-

[1]Adjusted 205-day weaning weight, kg

[2]Superscript letters denote least squares mean differences by Fisher's LSD

Dam genotype for XKR4 influenced A205 (p=0.0152) such that calves from AG dams had higher A205 (238 +/- 5 kg) than those from AA dams (232 +/- 4 kg). There was no interaction observed between season and dam XKR4 (p = 0.43).

Conclusion

These results suggest that dam genotype for DRD2 and XKR4 may influence calf A205, possibly through modulating effects of tall fescue toxicosis during lactation. This could indicate a potential for their use as genetic markers for increased productivity of beef cattle grazing endophyte-infected tall fescue.

References

Bastin, B. C., Houser, A., Bagley, C. P. et al. (Inpress). *Animal Genetics*.

Beef Improvement Federation. 2010.(9th Ed.). Raleigh, NC.

Ben-Jonathan N., Hnasko R. (2001). *Endocrinology Review* **22,** 724-63.

Campbell B. T., Kojima C. J., Cooper T. A., et al. (2014). *Animal Biotechnology*.

Cross D.L., Reinemeyer C.R., Prado J.C., et al. (2012). *J. Therio.* **78,** 1361-70.

Cutler A.J., Kalali A.H., Weiden P., et al. (2008). *J. Clin. Psychopharmacology* **28,** S20-28.

Fijal B.A., Stauffer V.L., Kinon B.J., et al. (2012). *J. Clin. Psychiatry* **73**,367-71.

Fribourg H.A., Gwinn K.D., Chestnut A.B., et al. (1991). *Tenn. Farm Home Sci.* **160,** 10-29.

Jain K.K. (2000). *Expert Opinions of Investigational Drugs* **9,** 2935-43.

Lavedan C., Licamele L., Volpi S., et al. (2009). *Molecular Psychiatry* **14,** 804-19.

Porter J. K., Thompson Jr. F. N. (1992). *J. Anim. Sci.* **70** no. 5 1594-03.

Porto Neto L.R., Bunch R.J., Harrison B.E., et al. (2012). *Animal Genetics* **43,** 785-9.

Schillo, K. K., Leshin L. S., Boling J. A., et al. (1988). *J. Anim. Sci.***66,** 713-8.

Stuedemann J.A., Hoveland C.S. (1988). *J. Prod. Ag.* **1,** 39-44.