Lorna G. Moore Research Interests

The period of pregnancy comprises one of the greatest physiological challenges experienced during the human lifespan. My research is concerned with the basic physiological processes by which women adjust to pregnancy, the impact of such developments on their own health and that of their offspring (both prenatally and later in life) and how such processes influence evolutionary adaptation. Distinctive features of these studies have been their vertically-integrated nature as well as use of the natural laboratory of residence at high altitude. High altitude has been chosen due to the fact that the chronic hypoxia exerts one of the greatest known depressant effects on fetal growth and further because human populations have resided at high altitudes for differing numbers of generations, thus providing an experiment of nature to determine whether evolutionary adaptation to high altitude has occurred.

Beginning some 25 years ago, our studies focused on the effects of pregnancy and sex steroids hormones on ventilation, ventilatory control during wakefulness and sleep, and blood volume. For the last 10 years, my work and that of my students has concentrated on the vascular effects of pregnancy and, more specifically, the factors responsible for raising maternal uterine artery blood flow nearly 100-fold during pregnancy. We have shown that such changes are due primarily to an increase in vessel diameter which is present well before the period of greatest blood flow rise. Interestingly, the increase in uterine artery diameter is greatly diminished in newcomer residents of high altitude but fully normal in populations with multiple generations of high-altitude residence (Andeans and Tibetans). In experimental animal studies, we have shown that chronic hypoxia alters uterine artery vasoregulatory as well as growth-related processes; specifically, reducing uterine artery nitric oxide production and vasodilator response to flow, decreasing DNA synthesis, and altering stress-strain relationships. In human populations residing in Colorado, Peru, Tibet and most recently Bolivia, we have shown that multigenerational high-altitude ancestry confers protection from the altitude-associated reductions in uterine artery blood flow and fetal growth.

My current research is proceeding in two related directions. In order to identify the genomic and genetic factors involved, we are using ~1 million single nucleotide polymorphisms gene chips technology to identify genomic regions associated with such protection. Several candidate regions have been identified. Oxygen-sensitive pathways appear disproportionately represented and these regions are being sequenced in order to identify the specific genes involved. The second direction concerns vasoreactivity studies in isolated uterine arteries in rodents and myometrial vessels obtained at the time of Cesarean section in order to determine the effects of normal and abnormal pregnancy on vasoregulation in this important vascular bed and specifically, whether K+ channels or other oxygen-sensitive pathways are implicated.

Five recent publications (from a total of over 190[1],:

1. Julian CG, Wilson MJ, Lopez M, Yamashiro H, Tellez W, Rodriguez A, Bigham A, Shriver M, Rodriguez C, Vargas E, **Moore LG.** Augmented uterine artery blood flow and oxygen delivery protect Andeans from altitude-associated reductions in fetal growth. Am J Physiol Regul Integr Comp Physiol. 2009 Feb 25. [Epub ahead of print].

[1] See pubmed, http://www.ncbi.nlm.nih.gov/sites/entrez but be aware that some publication listed for Moore LG are from L Gordon Moore

2. Julian CG, Galan HL, Wilson M, Desilva W, Cioffi-Ragan D, Schwartz J, **Moore LG.** Lower uterine artery blood flow and higher endothelin relative to nitric oxide metabolite levels are associated with reductions in birth weight at high altitude. Am J Physiol Regul Integr Comp Physiol. 2008 Sep;295(3):R906-15.
3. Bennett A, Sain SR, Vargas E, **Moore LG**. Evidence that parent-of-origin affects birth-weight reductions at high altitude. 2008 Am J Hum Biol. Sep-Oct;20(5):592-7
4. Shriver MD, Mei R, Bigham A, Mao X, Brutsaert TD, Parra EJ, **Moore LG**. Finding the genes underlying adaptation to hypoxia using genomic scans for genetic adaptation and admixture mapping. Adv Exp Med Biol. 2006;588:89-100.
5. Mateev S, Sillau AH, Mouser R, McCullough RE, White MM, Young DY, **Moore LG**. Chronic hypoxia opposes pregnancy-induced increase in uterine artery vasodilator response to flow. American Journal of Physiology: Heart and Circulatory Physiology, 284:H820-H829, 2003.

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