TDN: Dr. Chris Kawcak provided an insightful overview of musculoskeletal injury and the use of imaging biomarkers in diagnosis, and also spoke about the emerging evidence that the shape of a joint surface may be correlated to condylar fractures in the fetlock joint. How can biomarkers be used in predicting injury?

WM: A big part of our need is to monitor horses that are at risk of injury more than others. Our two potential means of doing that are with imaging--radiographs (X-ray) will only tell you so much--and fluid biomarkers.

In a study that we did in collaboration with Dr. Tim Parkin in the U.K., they did CTs of these horses that had fractures. We compared the fetlock joints of horses that had condylar fractures with the opposite fetlock joint in the same horse, then with fetlock joints from other Thoroughbreds that had died for other reasons that were the same age and had been on the racetrack, but hadn't fractured. What Dr. Chris Kawcak found was that there are significant differences in the joint geometry in the joints that fractured versus the joints that didn’t. We want to look at this further and see if they are made that way or if they develop over time that way. We have a hypothesis that it may be associated with certain procedures that bring the hoof around/change hoof direction. That’s the hypothesis--we certainly haven’t shown any proof on that yet. We have shown that there’s a significant difference in joint geometry in the horses that fracture though, but we haven’t shown why they get that difference in geometry, and that’s our next step.

The second offshoot of that research is that if we could do CTs, could we identify horses at risk that we can’t tell with just radiographs? That’s going to require a standing CT, so that’s an area of research that we need to get funded.

TDN: Dr. David Frisbie discussed a study completed in Southern California that was funded by the Grayson-Jockey Club Research Foundation where monthly blood samples were collected from 238 horses and showed that there was a 73.8% predictability in change in the biomarker panel predicting injury approximately six weeks beforehand. Talk a little bit about this study and the concept behind fluid biomarkers.

WM: The idea with fluid biomarkers is that they are more convenient because all you need is a blood sample for identifying the horse at risk, and you could have more strength to say to the owner or trainer that you need to do a CT or a bone scan. The fluid biomarkers are a bigger area [than imaging biomarkers] and have already received good funding. Most of the funding has come from private donors and also the Grayson-Jockey Club, which funded the study in California.

There are a number of sophisticated tests that can inform the track superintendent to add sand, increase moisture content, etc. I think we have a really good handle on how to make racetrack surfaces safe.
Bob Baffert, John Sadler, Richard Mandella and a number of other top trainers participated, so there were plenty of good horses involved in the study. In total, 238 2- and 3-year-old racehorses in training in California were used. When we got an injury, we looked at their biomarkers all the way back from the monthly samples in that group compared to matched controls--horses the same age/same sex--and it showed that we had a 73.8% predictability of injury, and that could be up to six weeks before.

So, we showed good predictability with the combination of seven biomarkers in that study, and going forward we'd like to make the test more like a blood chemistry test.

Hopefully, every month a horse's blood sample could be sent to the lab at a reasonable cost. We would want the cost to be less than $100. It's very similar to looking at profiles in the blood like we do for humans as far as identifying those at risk of heart attack, cardiovascular disease, etc. This is a huge area, and we really need funding to get testing together in a platform that the horsemen could use.

Fluid biomarkers are probably the only practical way of identifying horses at risk of injury. There's not too much else we could change other than not racing the horse to decrease risk. We should look at track surface, but the biomarkers could really identify the horse. At the moment, we've got to live with the fact that based on previous data, three out of 1,000 starters are going to have a fatal fracture on dirt and two out of a 1,000 on synthetics. And that varies, of course, depending on the make-up of the track.

Uniformity of track surface and predictive biomarkers are our two most likely potential helpers, and that's why we've already put a lot of energy and work into these areas. If you asked me to prioritize the greatest immediate need for funding, it would be in that area to help the prevention of injury.

**TDN:** The conventional therapies that are commonly used to treat joint injuries were also discussed at the conference, including physical therapy and rehabilitation, extracorporeal shock wave therapy, nonsteroidal anti-inflammatory drugs, intraarticular corticosteroids, hyaluronic acid, intraarticular/intramuscular Adequan, and Pentosan. Discuss some of these treatments and whether there are any out there that are proving to be more effective than others.

**WM:** Osteoarthritis has been estimated to be the reason that 60% of our equine athletes retire. It doesn't kill them, but it causes them to stop racing. It's obviously a hugely important area. The current therapies that we use routinely are intraarticular corticosteroids, hyaluronic acid, and Adequan, and they are all useful. We certainly differentiated that Depo Medrol is not good for the joints, where the other commonly used ones are OK.

We have shown in our research that Pentosan, intramuscularly, is better than Adequan, but it's not licensed in the U.S. yet. We're not saying that using Adequan intramuscularly is useless, though. Adequan still has a question mark on it, but there are people who feel that they see a difference when their horses are on it. We just haven't been able to show it scientifically yet. We haven't shown that intramuscularly at that dose [500mg] that it could successfully change the Osteoarthritis that is there.

We have shown that with Pentosan, and that's why I'm quite excited about us getting it licensed in the U.S. It's commonly used in Australia, New Zealand and France--just not here yet. We need funding to complete these studies.

**TDN:** Dr. Frisbie also discussed the emerging biological musculoskeletal therapies, including natural anti-inflammatory protein (IRAP), mesenchymal stem cells, and Platelet Rich Plasma (PRP). What is the current state of research in this field?

**WM:** We've shown IRAP to be a definite benefit, and sometimes it benefits joints that don't respond to corticosteroids. They are getting used increasingly and they're a good biological healing type therapy rather than just using anti-inflammatory products. These kind of products are the future because it's providing a benefit to the horse and not just enabling it to race. We've validated the use of IRAP, and I think a lot of people are very comfortable using it. It's used more in France and England where they have more restrictions on corticosteroid use.

We still have a lot to learn about stem cells as far as what's the best way of manipulating them, identifying them as true stem cells, and getting good evidence that they significantly improve over other therapies the ability to heal tendons, ligaments and joints. We've got pretty good evidence in joints that stem cells are beneficial for healing soft tissue damage, as well as ameliorating osteoarthritis.

Based on the studies that we've published, bone marrow-derived stem cells are better than fat-derived stem cells. We've also found that with bone marrow derived stem cells, that it doesn't matter how old the horse is. In other words, an older horse can still have good stem cells cultured and put back into their joints, tendon or suspensory injuries. We just recently submitted a paper where we've shown that there's a significant improvement in re-injury rate [less re-injury] with stem cells in tendons repair compared to the standard of care before that. We're pretty excited about bone marrow derived stem cells. We just have to be careful about the indications and that's where further research comes in.

**TDN:** Closing thoughts?

**WM:** Of all the issues to racing that negatively effect us, the number one is fatal musculoskeletal injury. The priorities need to be early detection of disease that leads to injury, and more effective treatments of that disease. You diagnose it early and treat it early before it's irreversible. I think that's really the bottom line.
The care and safe keeping of our equine athletes is this industry's primary concern. Research money is hard to come by since the downturn in 2007. At Pegasus Thoroughbred Rehabilitation and Training Center, I have been funding studies on Osteoarthritis following surgery and the use of Platelet Rich Plasma and stem cells with Dr. McIlwraith and Colorado State University. Research takes time and we need to get more of our equine researchers back doing research on E.I.P.H., racetrack surfaces, biomarkers and stem cells. We need to find a way to fund this research now and into the future.