

### This week in therapeutics

| Indication            | Target/marker/pathway                           | Summary  | Licensing status  | Publication and contact information  |
|-----------------------|---|--|---|--|
| <b>Inflammation</b>   |   |  |   |  |
| Inflammatory diseases | Microsomal prostaglandin E synthase-1 (mPGES-1) | A structural study of mPGES-1 could aid the design of mPGES-1 inhibitors to treat inflammation. Electron crystallography of 2D crystals in the presence of glutathione and phospholipid cofactors revealed the enzyme's conformation during the synthesis of proinflammatory prostaglandin E <sub>2</sub> (PGE <sub>2</sub> ). The structural model suggests that glutathione binds between the enzyme's three subunits and reduces the precursor molecule prostaglandin H <sub>2</sub> to PGE <sub>2</sub> . Next steps include identifying compounds that stabilize the closed conformation of mPGES-1 to block catalysis. Orexo AB and Boehringer Ingelheim GmbH are jointly developing mPGES inhibitors to treat pain, inflammation and rheumatoid arthritis (RA). | Patent application filed for the structural conformation; structure tools are in use in-house and discussions are ongoing with potential partners; licensing status undisclosed | Jegerschold, C. <i>et al. Proc. Natl. Acad. Sci. USA</i> ; published online Aug. 4, 2008; doi:10.1073/pnas.0802894105<br><b>Contact:</b> Hans Hebert, Karolinska Institute, Stockholm, Sweden<br>e-mail: <a href="mailto:hans.hebert@ki.se">hans.hebert@ki.se</a><br><b>Contact:</b> Per-Johan Jakobsson, same affiliation as above<br>e-mail: <a href="mailto:per-johan.jakobsson@ki.se">per-johan.jakobsson@ki.se</a><br><b>Contact:</b> Caroline Jegerschöld, same affiliation as above<br>e-mail: <a href="mailto:caroline.jegerschold@ki.se">caroline.jegerschold@ki.se</a> |