

lighter vitellogenin form has been found in the hypopharyngeal glands of workers, where vitellogenin constituents are processed into food secretions for larval feeding (Amdam et al. 2003a). This lighter vitellogenin is not found in the unexposed honey bee brain (Fig. 2B, 3B). As nurse bees show higher vitellogenin titers and are responsible for the feeding of the larvae (Amdam et al. 2003a, b), the lighter vitellogenin in the brain may be a marker of nurse bees. The exposure of foragers to clothianidin induced the light vitellogenin in the foragers, suggesting the presence of a “nurse-bee”-like phenotype. Vitellogenin plays such an essential role in hormone signalling and in transition of nurse bees, which have high vitellogenin levels, to foragers, which have lower vitellogenin levels. Vitellogenin is also involved in stress management by protecting against oxidative stress and regulation of life-span; long-lived queens show high vitellogenin levels (Amdam et al. 2004b, Nelson et al. 2007, Seehuus et al. 2006). On this basis, we conclude that altered levels of vitellogenin may have significant physiological consequences in exposed worker bees. Further studies are needed to link vitellogenin alteration to physiological outcomes and to demonstrate whether vitellogenin may serve as a biomarker candidate for the exposure of honey bees to neonicotinoids and other pesticides. It should be noted that possibly other factors may also affect vitellogenin protein levels and that they may fluctuate or become increased in a compensatory manner, or induction may be transient. More detailed investigation should thus be devoted to such questions before vitellogenin can be regarded as a biomarker for pesticide exposure. The advancement of our newly developed antibody is the fact that it represents a good tool to analyse in detail the physiological role of vitellogenin in honey bees and to analyse the potential effects of plant protection products on vitellogenin expression and function.

## REFERENCES

- Amdam GV, Norberg K, Hagen A, Omholt SW. 2003a. Social exploitation of vitellogenin. PNAS. 100 (4): 1799-1802.
- Amdam GV, Omholt SW. 2003b. The hive bee to forager transition in honeybee colonies: the double repressor hypothesis. J Theor Biol. 223 (4): 451-464.
- Amdam GV, Hartfelder K, Norberg K, Hagen A, Omholt SW. 2004a. Altered physiology in worker honey bees (Hymenoptera: Apidae) infested with the mite *Varroa destructor* (Acari: Varroidae): a factor in colony loss during overwintering? J. Econ. Entomol. 97: 741-747.
- Amdam GV, Norberg K, Fondrk MK, Page RE. 2004b. Reproductive ground plan may mediate colony- level selection effects on individual foraging behavior in honey bees. PNAS. 101: 11350–11355.
- Antúnez K, Martín-Hernández R, Prieto L, Meana A, Zunino P, Higes M. 2009. Immune suppression in the honey bee (*Apis mellifera*) following infection by *Nosema ceranae* (Microsporidia). Environ. Microbiol. 11 (9): 2284-2290.
- BenVau LR, Nieh JC. 2017. Larval honey bees infected with *Nosema ceranae* have increased vitellogenin titers as young adults. Sci. Rep. 7 (1): 14144.
- Blank S, Seismann H, McIntyre M, Ollert M, Wolf S, Bantleon FI, Spillner E. 2013. Vitellogenins are new high molecular weight components and allergens (Api m 12 and Ves v 6) of *Apis mellifera* and *Vespula vulgaris* venom. PLoS. One. 8 (4): e62009.
- Chen ME, Lewis DK, Keeley LL, Pietrantonio PV. 2004. cDNA cloning and transcriptional regulation of the vitellogenin receptor from the imported fire ant, *Solenopsis invicta burren* (Hymenoptera: Formicidae), Insect. Molecul. Biol. 13: 195-204.
- Christen V, Duong F, Bernsmeier C, Sun D, Nassal M, Heim MH. 2007. Inhibition of alpha interferon signaling by hepatitis B virus. J. Virol. 81 (1): 159-165.