

# *Paeonia Suffruticosa* root bark extract in combination with the $\alpha$ -MSH biomimetic peptide Greyverse™ stimulates pigmentation in human hair follicles.

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473

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## Introduction:

Canities is an age-linked loss of bulb melanocyte and hair follicle (HF) pigmentation. It can significantly alter the physical appearance of a person and negatively impact their well-being, which drives the search and demand for anti-greying agents. Our preliminary studies revealed that *Paeonia Suffruticosa* root bark extract (PS) in combination with the  $\alpha$ MSH biomimetic synthetic peptide Greyverse™ synergically induces mitochondrial E3 ligase (MITOL) and melanogenesis in human melanocytes in vitro.  $\alpha$ MSH is a pro-pigmentary hormone of the melanocortin family, which stimulates melanogenesis through its target receptor, MC1R. Gv is an established promoter of HF melanogenesis with redox properties. This study investigated the additive effects of PS and Gv on hair pigmentation ex vivo.

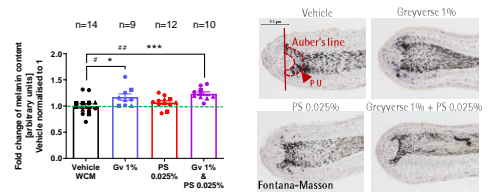
## Materials & Methods:

Human microdissected HFs were cultured for 4 days in serum-free medium, supplemented with vehicle, Gv, PS or Gv + PS (systemic treatment). Afterwards immunohistochemistry was performed to assess melanin content (Fontana-Masson). Additionally, activity of tyrosinase, the rate-limiting enzyme of melanin synthesis, expression of tyrosinase-related protein 1 (TYRP), the pre-melanosome protein Gp100, and  $\alpha$ MSH were examined by quantitative (Immu-)histomorphometry.



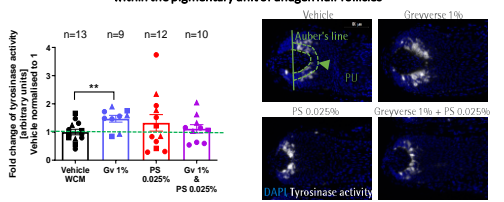
## Results & Discussion:

### PS tententially, Gv and the combination of Gv and PS significantly boosted melanin content within the pigimentary unit of anagen hair follicles



The co-treatment of Gv and PS boosted melanin content within the pigimentary unit of the hair follicle. Relative intensity of melanin content (left) and representative images of the results obtained from three donors after systemic treatment with Gv and PS (right). Data are presented as mean +/- SEM, representing a total of 9-14 anagen hair follicles from three donors. Kruskal Wallis Test (#) and Mann Whitney U Test (\*) were used to statistically compare the different treatment groups. PU = pigimentary unit.

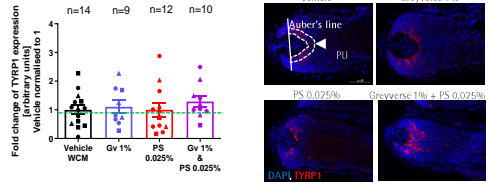
### PS tententially, Gv and the combination of Gv and PS significantly boosted melanin content within the pigimentary unit of anagen hair follicles



Gv treatment significantly increased tyrosinase activity within the pigimentary unit of the hair follicle. Relative intensity of tyrosinase activity (left) and representative images of the results obtained from three donors after systemic treatment with Gv and PS (right). Data are presented as mean +/- SEM, representing a total of 9-13 anagen hair follicles from three donors. Kruskal Wallis Test (#) and Mann Whitney U Test (\*) were used to statistically compare the different treatment groups. PU = pigimentary unit.

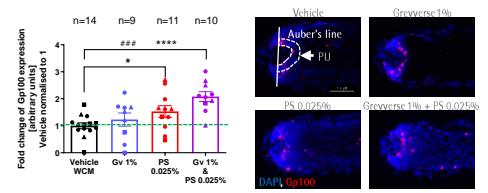
## Results & Discussion:

### The combination of Gv and PS resulted in a synergistic trend stimulating tyrosinase-related protein 1 (TYRP) expression



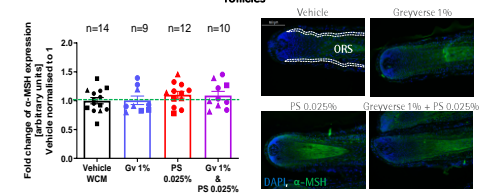
The co-treatment of Gv and PS showed tendential additive effects of TYRP within the pigimentary unit of the hair follicle. Relative intensity of TYRP expression (left) and representative images of the results obtained from three donors after systemic treatment with Gv and PS (right). Data are presented as mean +/- SEM, representing a total of 9-14 anagen hair follicles from three donors. Kruskal Wallis Test (#) and Mann Whitney U Test (\*) were used to statistically compare the different treatment groups. PU = pigimentary unit.

### PS alone, and Gv and PS synergistically increased Gp100 expression within the pigimentary unit of anagen hair follicles



The treatment with PS and co-treatment of Gv and PS had synergistic effects on Gp100 within the pigimentary unit of the hair follicle. Relative intensity of Gp100 expression (left) and representative images of the results obtained from three donors after systemic treatment with Gv and PS (right). Data are presented as mean +/- SEM, representing a total of 9-14 anagen hair follicles from three donors. Kruskal Wallis Test (#) and Mann Whitney U Test (\*) were used to statistically compare the different treatment groups. PU = pigimentary unit.

### PS tententially increased $\alpha$ -MSH expression within the outer root sheath of anagen hair follicles



PS containing treatments increased  $\alpha$ -MSH within the outer root sheath of the hair follicle. Relative intensity of  $\alpha$ -MSH expression (left) and representative images of the results obtained from three donors after systemic treatment with Gv and PS (right). Data are presented as mean +/- SEM, representing a total of 9-14 anagen hair follicles from three donors. Mann Whitney U Test (\*) were used to statistically compare the different treatment groups. ORS = outer root sheath.

## Conclusions:

Taken together, Gv and PS showed synergistic effects in promoting hair pigmentation, possibly primarily via stimulating melanosome production/maturation. Thus, this combinational treatment deserves further pre-clinical and clinical exploration for the reversal of hair greying.

## References:

1) Scalvino et al (2018) *Int J Cosmet Sci. Efficacy of an agonist of  $\alpha$ -MSH, the palmitoyl tetrapeptide-20, in hair pigmentation.* 2) Hardman et al (2015) *J Invest Dermatol. The peripheral clock regulates human pigmentation.* 3) Tobin (2011) *Pigment Cell Melanoma Res. The cell biology of human hair follicle pigmentation.*