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## Characterization of olfactory receptors expression in BON cells

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► **To cite this version:**

Guenhaël Sanz, Aurélie Dewaele, Edith Pajot. Characterization of olfactory receptors expression in BON cells. *Congres of the European Chemoreception Research Organization, Sep 2009, Cagliari, Italy. 2009.* ⟨hal-02812011⟩

**HAL Id: hal-02812011**

**<https://hal.inrae.fr/hal-02812011v1>**

Submitted on 6 Jun 2020

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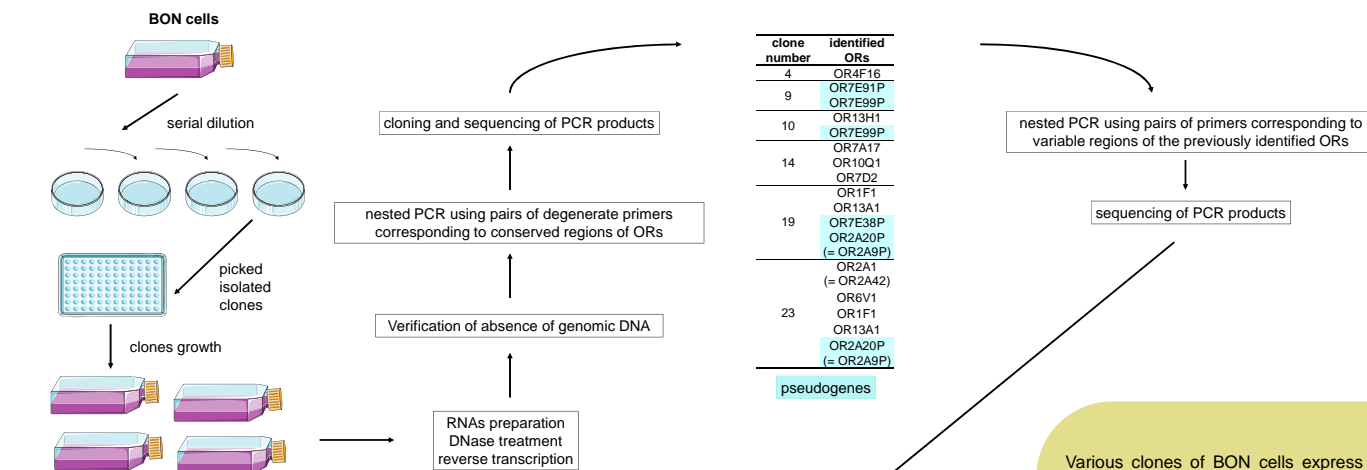
HAL Authorization

BON cells are a cell line derived from human enterochromaffin cells. They were previously described to express various olfactory receptors (ORs), but it is unclear whether a single cell expresses several types of ORs, as reported for spermatogenic cells, or a single type of OR as for olfactory sensory neurons (OSNs). The goal of the present work was first to answer this question and secondly to explore whether BON cells could be used for functional studies of heterologously expressed ORs.

BON cells were kindly provided by Kirk Ives (UTMB Galveston, USA). As the cell population appears heterogeneous in terms of morphology, we first serially diluted BON cells to isolate clones. RT-PCR was then carried out on RNAs from clones. RT-PCR products were subsequently cloned and sequenced. Clonal BON cells appear to express more than one OR and some ORs identified are expressed by several clones. To confirm the expression of several olfactory receptors by a single cell, single-cell RT-PCR was also performed.

Since BON cells endogenously express ORs, we expected they could also efficiently express heterologous ORs, which is still a challenge for most ORs in mammalian cells. Thus, we tried to heterologously express two human ORs (OR1G1 and OR17-40) in BON cells. We demonstrated that BON cells efficiently expressed these olfactory receptors at the plasma membrane level. Furthermore, we conducted calcium imaging and confirmed the activation of both receptors by their known ligands. While other ORs should be tested for functional expression by BON cells, these first results already suggest that BON cells constitute an interesting means to carry out functional studies of heterologously expressed ORs.

## Endogenous expression of olfactory receptors by BON cells

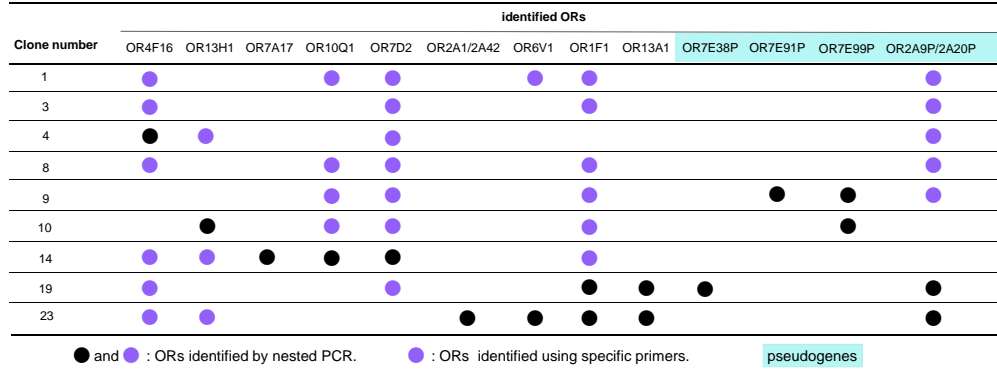


Various clones of BON cells express various groups of ORs, but a subset of ORs (OR7D2, OR1F1) is common to most of the clones.

BON cells also express pseudogenes at the mRNA level.

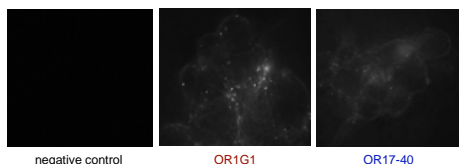
Both OR7E38P and OR2A9P pseudogenes, as well as OR7A17, OR7D2 and OR2A1 are reported to be expressed in several tumors.

Clones of BON cells could have derived with time. We confirmed that single BON cells can indeed express several ORs using single-cell RT-PCR and specific primers targeting some of the previously identified ORs. We did not succeed in detecting all the receptors we were looking for. Nevertheless, we found that single cells of clone 14 co-express OR4F16 and OR10Q1.

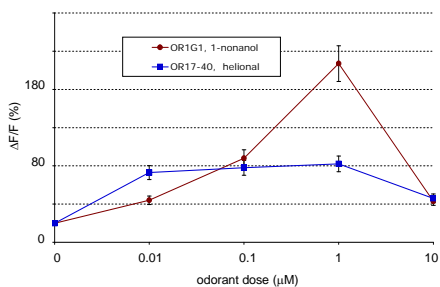


## Functional heterologous expression of olfactory receptors by BON cells

BON cells were transiently transfected with mammalian expression vectors carrying the OR1G1 or OR17-40 receptor. Cells were observed 72h after transfection.



BON cells heterologously express human OR1G1 and OR17-40 receptors. The receptors are fused to the c-myc epitope at their N-terminal end. They are revealed with an anti-cmyc antibody coupled to Cy3 on non permeabilized cells.



BON cells expressing OR1G1 or OR17-40 were loaded with fluo-4 and stimulated with various concentrations of cognate ligands of these ORs. They displayed a calcium response within seconds when the ligand of the expressed OR was applied, while mock-transfected BON cells did not.

## Conclusion

Contrary to OSNs, BON cells were shown to endogenously co-express various functional ORs and pseudogenes at the mRNA level. While some receptors appear to be expressed by all cells, each clone of BON cells seems to express a specific panel of ORs.

In the olfactory apparatus, a combinatorial code is used to detect and discriminate odorants, involving several OSNs each expressing a single type of OR. In the case of BON cells, the variability in OR expression and the ability to co-express several ORs could be used for the detection of various odorants or other molecules brought by food intake into the gastro-intestinal tract.

Furthermore, we demonstrate that BON cells can express functional heterologous ORs. Thus, BON cells seem promising for contributing to the deorphanization of ORs and their functional study.