

(pre-)Clinical research to understand alopecia and improve scalp cooling results

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Background

- Authors: international multi-disciplinary special interest group (SIG) on chemotherapy-induced alopecia (CIA) & scalp cooling
- Pathobiology of CIA is still not fully understood¹
- Prevention of CIA by scalp cooling (Fig 1):
 - o Well tolerated by patients
 - o Overall 50% satisfactory results
 - o Increasingly used world wide
- Goal of SIG: study CIA by combining pre-clinical & clinical research, ultimately improving efficacy of scalp cooling

Methods

Study mechanism of CIA & preventative role of cooling:

- Studying in vitro cell toxicity models, using a variety of cultured keratinocytes (including human hair follicular keratinocytes, normal epidermal human keratinocytes & immortalised human keratinocytes)
- Clinical investigation into the role of post-infusion scalp cooling times (PICT) & scalp skin temperature on severity of CIA
- Investigate intracellular pathways mediating damage to human hair follicle-associated cell populations

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References: ¹Paus R et al. Pathobiology of chemotherapy-induced hair loss. *The Lancet Oncology*. 2013; 14: e50-9 | ²Al-Tameemi W et al. Use of in vitro human keratinocyte models to study the effect of cooling on chemotherapy drug-induced cytotoxicity. *Toxicology in vitro*. 2014; 28: 1366-76 | ³Komen M et al. Results of 20 versus 45 minutes post-infusion scalp cooling time in the prevention of docetaxel-induced alopecia (2015, submitted) | ⁴Komen M et al. Results of scalp cooling during anthracycline chemotherapy in relation with scalp skin temperature (2015, submitted)

Results

- Cooling rescues cells in culture from cytotoxicity caused by doxorubicin, docetaxel & the active metabolite of cyclophosphamide (4-OH-cyclophosphamide) (Fig 2 & 3).² Observations are extended to series of other commonly used chemotherapy drugs, e.g. paclitaxel
- No significant differences in CIA found for PICTs of 90, 45 & 20 minutes in 3-weekly docetaxel chemotherapy (75 or 100 mg/m²).³ Degree of CIA is temperature dependent, best results for anthracyclines obtained at temperatures <20°C⁴
- A feasible method to determine P53 in hair follicle-associated cell populations has been developed

Discussion/ Conclusion

- Cooling reduces cell death when exposed to a range of chemotherapeutic drugs, reflecting clinical outcomes
- Dose is a determining factor, but half-life times of cytotoxics do not seem to be the most important factor for the optimal PICT
- Adapting scalp cooling temperatures to individual scalp skin temperatures could enhance results
- Combining pre-clinical & clinical research supports development of a patient tailored approach with the ultimate goal to prevent CIA for our patients & thereby improve their quality of life

OH is part time researcher at Paxman Coolers Ltd. Other authors declare to have no conflict of interest. SIG meetings are hosted by Paxman Coolers Ltd.



Figure 1: scalp cooling

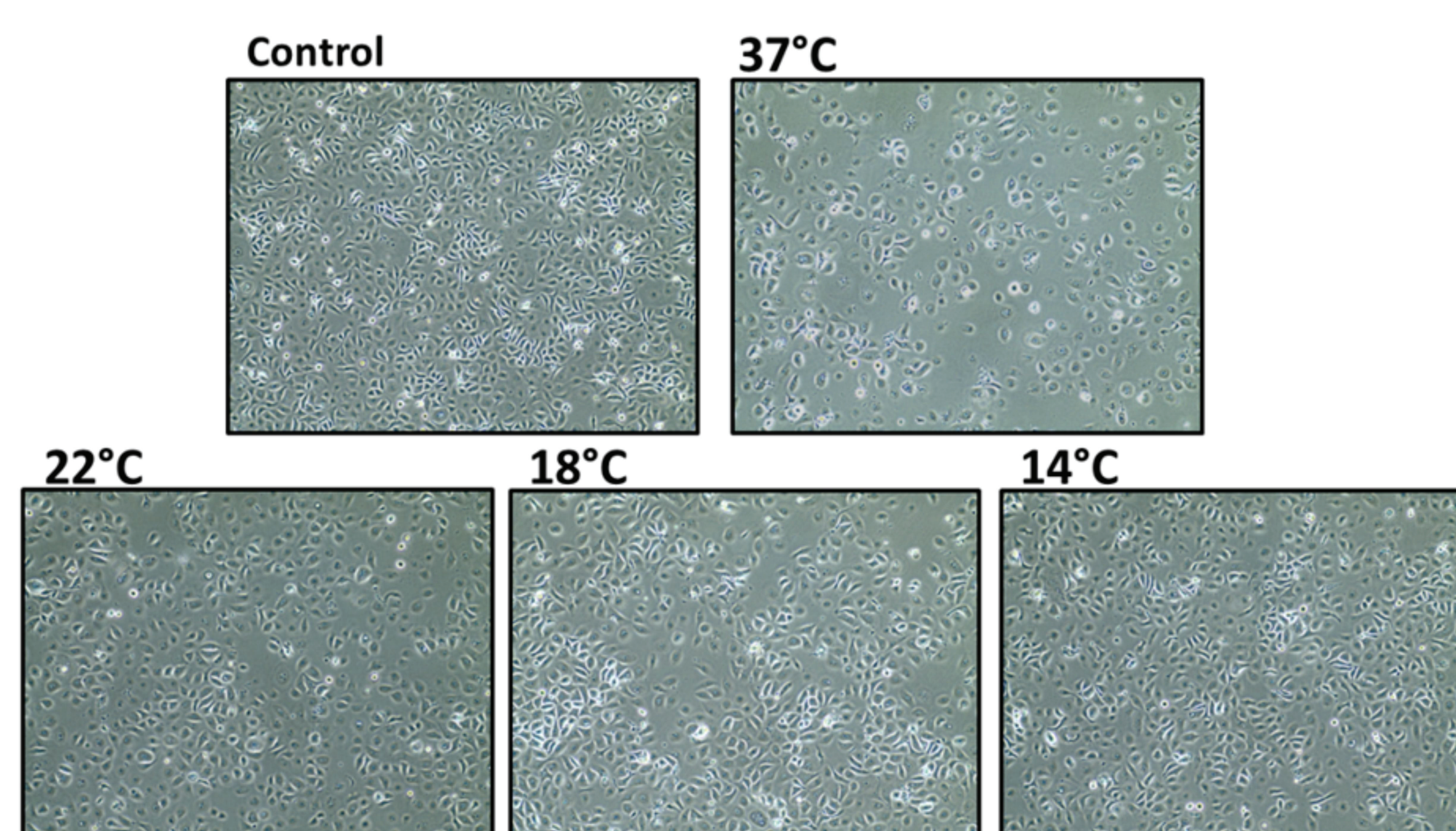


Figure 2: HaCaTa cells treated with 0.5 µg/ml doxorubicin at 37°C, 22°C, 18°C & 14°C for 2 hours. Viability assessed by phase contrast microscopy 72 hours post drug treatment

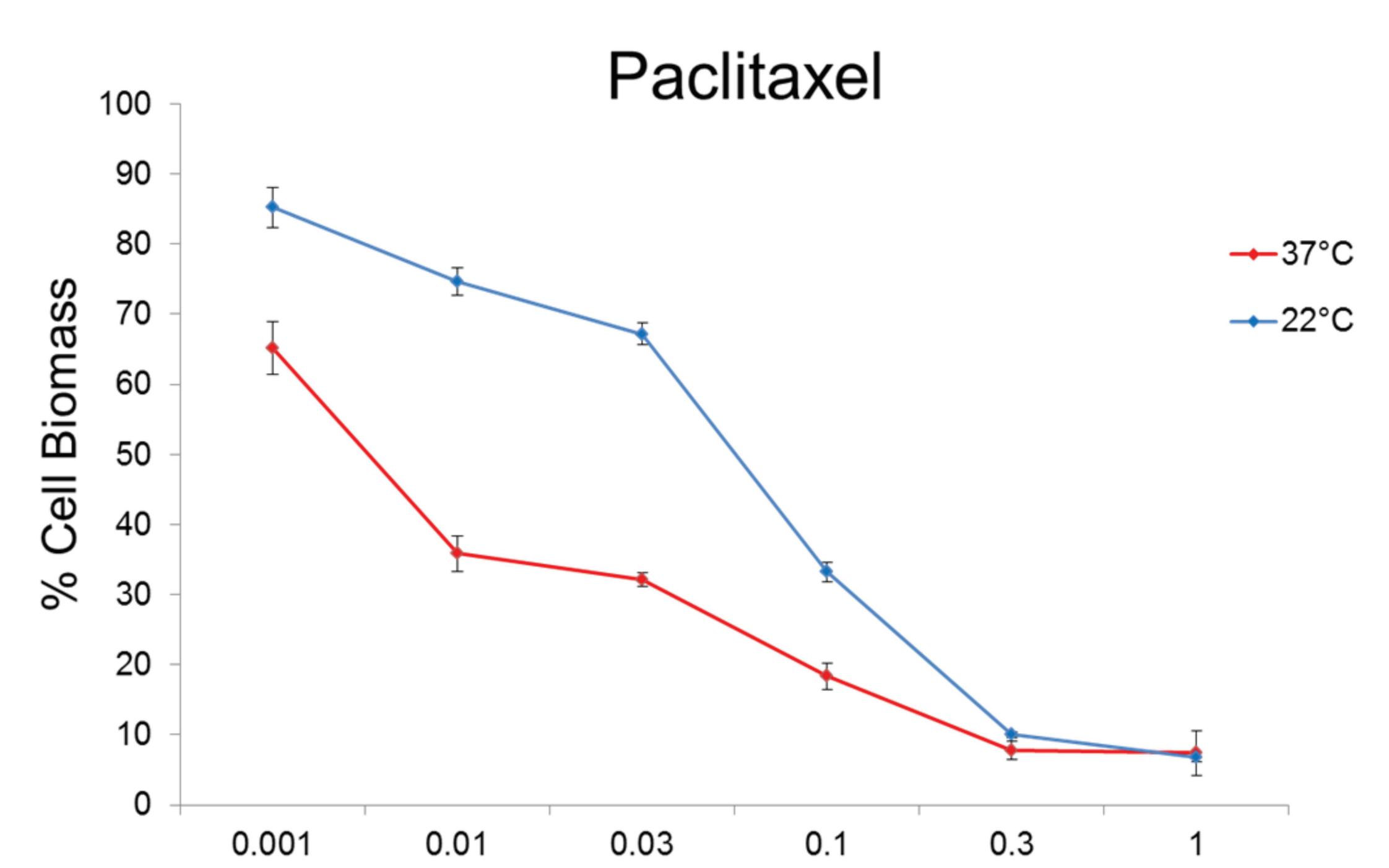


Figure 3: HaCaTa cells treated with indicated doses of paclitaxel for 2 hours at 37°C & 22°C. Viability assessed by measuring bio-mass (% with respect to control cultures) 72 hours post treatment