Impact of amino acids or other compounds on the synthesis of melanin

Melanin can be synthesized through air-mediated oxidation of a catecholic or indolic compound under alkaline conditions. Despite the simplicity of this reaction, a complete description of the chemistry and an explanation of the physical properties of melanins is lacking. An obvious physical characteristic of melanins is their capacity to absorb light over a broad range of the electromagnetic spectrum leading to their characteristic dark appearance. However, it is unclear whether this dark appearance is due to chemical or physical features of the material. Melanin-like materials can be synthesized from a wide variety of precursors. Depending on the precursor involved and the reaction conditions, materials with different physical appearances, e.g., dark brown to black vs. light brown to yellow, can be generated. Earlier observations indicated that the presence of cysteine in the reaction mixture leads to materials with much darker appearances. These earlier observations were expanded through the testing of 1) other amino acids, e.g., methionine, 2) amino acid derivatives, e.g., tryptamine, and 3) protein. The goal of the experiments was to determine if the addition of such compounds would impact the appearance, lighter or darker in color, of the melanin-like material synthesized. Our experiments indicated that the addition of some additives to the reaction leads to an increased precipitation of melanin. These observations could have significant impacts on the ability of melanin to coat surfaces. The potential applications of these findings will be discussed.
Drug enantiomers can have different effects on the human body, varying in bioavailability and potency. In the famous case of thalidomide, one enantiomer can alleviate morning sickness during pregnancy while its chiral counterpart causes birth defects during gestation. The thalidomide crisis highlights the tragic consequences of enantiomeric differences in drug biological activity and underscores the importance of developing rapid analytical techniques for enantiomeric discrimination. Popular methods for enantiomer differentiation are limited by high sample consumption, long analysis times, and low sensitivity. Ion mobility-mass spectrometry (IM-MS) enables rapid gas-phase separation of many isomeric and isobaric compounds, but small molecular enantiomers share many chemical and physical properties, making them a famously difficult class of molecules to separate. A potential avenue to overcome this challenge is the use of chiral shift reagents which can interact enantioselectively with the two chiral forms of a drug to impart measurable structural differences. This noncovalent complexation can render the two forms directly resolvable using IM-MS. Our previous work explored copper-amino acid complexes as chiral selectors, and current work seeks to complement this data by investigating beta-cyclodextrin’s capacity to separate chiral drugs. Recent literature suggests the unique properties of β-cyclodextrin (βCD) show great potential in enantiomeric differentiation through the utilization of a host-guest mechanism for chiral selection. βCD has been demonstrated to enantioselectivity complex amino acid enantiomers, rendering them differentiable by ion mobility-mass spectrometry (IM-MS). Thus, this study will assess the separation capacity of βCD for pharmaceutical drug enantiomers such as thalidomide.
3. Camille Haskins  
Senior  
Biology  
Tennessee State University  
Hannah Barge* MS, Sarika Saraswati** PhD  
Dina Hassan* MD, Vanderbilt University Medical Center  

Wnt signaling inhibition promotes wound healing and inhibits fibrosis in chronic wounds

Wnt signaling is activated following acute cutaneous injury and promotes fibrotic wound healing. Topical application of Wnt signaling inhibitors promotes regenerative cutaneous repair following acute injury. However, there is a gap in our understanding of Wnt signaling activation in chronic non-healing human wounds. This work is focused on delineating the impact of canonical Wnt signaling modulation in chronic wounds. Preliminary studies in our lab have shown that full-thickness excisional wounds in Streptozotocin (STZ)-induced type I diabetic mice activated Wnt signaling in both dermal and epidermal layers identified by β-catenin immunostaining and AXIN 2 transcript levels. Treatment with Wnt signaling inhibitors promoted regenerative repair following an excisional wound. Analysis of a panel of human chronic wound pathologies demonstrated differential expression of β-catenin in different chronic wounds. To understand the cellular mechanism of Wnt signaling modulation in Wnt-responsive chronic wounds, we treated human diabetic fibroblasts with Wnt signaling inhibitors and performed Western blot analysis for active β-catenin protein. Wnt signaling inhibitors ICG-001 and XAV-939 inhibited the expression of a pro-fibrotic protein, Collagen 1a1 together with active β-catenin. Future work will focus on analyzing the functional effect of Wnt signaling inhibitors on diabetic fibroblasts. These results suggest that Wnt signaling inhibitors could be utilized for the treatment of Wnt-responsive chronic wounds. Our goal is to identify the cellular and molecular players of fibrotic wound healing that can be modulated by Wnt signaling inhibitors. Our studies will pave the way to using Wnt signaling inhibitors for selective personalized therapy for chronic wounds.
4. Danielle Jathan  
Junior  
Biology  
Lemoyne Owen College  
Dr. Mark Kahn  
Oral  

“Investigating proliferation of murine placental endothelial cells in vivo”

During gestation, the placenta serves as a temporary but invaluable link between the mother and fetus, mediating nutrient and oxygen exchange to the conceptus and subsequently preserving its capacity for normal development. Placental dysfunction can lead to many severe pregnancy complications, such as preeclampsia and intrauterine growth restriction (IUGR). Therefore, understanding the mechanisms of placental development is crucial to better address these complications and ultimately ensure successful pregnancy outcomes. Furthermore, endothelial cells (EC) play a significant role in vascularizing the placenta to facilitate nutrient and oxygen exchange between maternal and fetal blood. Understanding both normal and abnormal mammalian development requires specific knowledge of ECs; however, the mechanisms that govern placental EC functionality and behavior are not well understood. Particularly, there is a lack of information addressing the timing, rates, and extent to which EC proliferation occurs at different developmental stages. Therefore, this project aims to explore these characteristics in vivo, using the wildtype murine placenta. Click-iT EdU assay and other proliferating markers were applied to visualize proliferating cells in placentas at both early (E11.5) and late (E15.5) gestational timepoints. Different conditions of EdU administration to pregnant dames were also considered, which helped to gain insight into the timing of placental cell cycles. The results suggested that most proliferating cells detected in the placenta were non-endothelial and rather of trophoblast origin, with proliferation signals expressing relatively higher at the early gestational timepoint. For future directions, this information can be used to compare cell proliferation in mutant placentas to characterize phenotypes.