THE GUIDANCE OF OLFACTORY SENSORY AXONS TO IDENTIFIABLE PROTOGLOMERULI IN THE LARVAL ZEBRAFISH OLFACTORY BULB

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ABSTRACT

THE GUIDANCE OF OLFACTORY SENSORY AXONS TO IDENTIFIABLE PROTOGLOMERULI IN THE LARVAL ZEBRAFISH OLFACTORY BULB

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During development, sensory neurons in the olfactory epithelium extend axons into the olfactory bulb. The earliest axons to enter the bulb terminate onto distinct neuropilar condensations called protoglomeruli. Protoglomeruli are thought to segregate into individual glomeruli later in development. The three day old larval zebrafish olfactory bulb contains 12 stereotyped, identifiable protoglomeruli, rendering it a good system to investigate mechanisms of initial axonal targeting in the bulb. In this thesis, I describe the generation of transgenic zebrafish lines in which neurons expressing odorant receptors along with the olfactory marker protein (OMP), V2R vomeronasal receptors along with the transient receptor potential channel2 (TRPC2) or the odorant receptor OR111-7 are selectively labeled. OMP and TRPC2 expressing neurons innervate multiple, non-overlapping protoglomeruli. Transgenic neurons expressing OR111-7:IRES:Gal4; UAS:Citrine transgenes primarily target a single protoglomerulus, the central zone, allowing the investigation of mechanisms directing axonal navigation to an individual protoglomerulus. Using this transgenic line, I show for the first time in any system that netrin/DCC signaling is required to guide olfactory sensory axons to a specific location within the olfactory bulb. Interestingly, I find that the central zone protoglomerulus is innervated by neurons expressing related odorant receptors of the OR111 subfamily. Upon replacing the coding sequence of OR111-7 in the OR111-

7:IRES:Gal4 transgenic construct with RFP, axons continue to target the central zone, suggesting that the OR111-7 is not required for the protoglomerular targeting of transgene expressing axons. Rather, it is likely that the transgenic construct is selectively expressed in neurons destined to target the central zone. Based on these observations, I propose a model hypothesizing that the zebrafish olfactory epithelium consists of distinct neuronal subsets. Each subset innervates a specific protoglomerulus and is restricted to express a predetermined set of odorant receptors and axon guidance receptors, which mediate the navigation of axons to particular protoglomeruli. These studies have laid the groundwork for future investigations into the mechanisms of axonal targeting to protoglomeruli in the larval zebrafish olfactory bulb.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES